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U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

Examiner # (Mandatory): 68363 Requester's Full Name: RUSSELL TRAVERS PRIMARY EXAMINER GROUP 1200

Art Unit 1617 Location (Bldg/Room#): CM1/2A11 2B19 Phone (circle 305 306 308) 4603

Serial Number: 09/709383 Results Format Preferred (circle): PAPER DISK E-MAIL

Title of Invention Dipeptide peptides Dimers + methods of making + use

Inventors (please provide full names): Paul Jackson & Joseph Stein

Earliest Priority Date: 12/11/99

Keywords (include any known synonyms registry numbers, explanation of initialisms):

Isoleucine, Statine, Leucine

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MAR 14 21
(STIC)

Search Topic:

Please write detailed statement of the search topic, and the concept of the invention. Describe as specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples of relevant citations, authors, etc., if known. You may include a copy of the abstract and the broadcast or most relevant claim(s).

See claim 26 for methods + claim 4 for compounds

POINT OF CONTACT:
PAUL SCHULWITZ
TECHNICAL INFO. SPECIALIST
CM1 6B06 TEL. (703) 305-1954

STAFF USE ONLY

Searcher: Paul Schulwitz
Searcher Phone #: _____
Searcher Location: _____
Date Picked Up: 3/15
Date Completed: 3/26
Clerical Prep Time: 60
Terminal Time: _____
Number of Databases: _____

Type of Search

_____ N.A. Sequence
_____ A.A. Sequence
1 Structure (#)
_____ Bibliographic
_____ Litigation1
_____ Fulltext
_____ Procurement
_____ Other

Vendors (include cost where applicable)

✓ STN
_____ Questel/Orbit
_____ Lexis/Nexis
_____ WWW/Internet
_____ In-house sequence systems (list)
_____ Dialog
_____ Dr. Link
_____ Westlaw
_____ Other (specify)

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L6                STR
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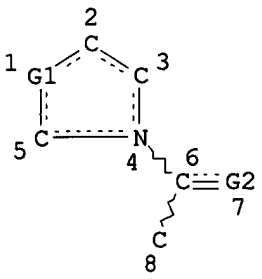


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VAR G2=O/S
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   1
NUMBER OF NODES IS   8

STEREO ATTRIBUTES: NONE
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                 NCOC2/ES OR NCSC2/ES
L10       256512 SEA FILE=REGISTRY SUB=L8 SSS FUL L6
L11            9 SEA FILE=REGISTRY ABB=ON  PLU=ON  ("DIPEPTIDYL PEPTIDASE
                 IV"/CN OR "DIPEPTIDYL PEPTIDASE IV (CAULOBACTER CRESCENTUS
                 GENE CC2154)"/CN OR "DIPEPTIDYL PEPTIDASE IV (FLAVOBACTERIUM
                 MENINGOSEPTICUM CLONE PFDP-10 SUBUNIT)"/CN OR "DIPEPTIDYL
                 PEPTIDASE IV (PORPHYROMONAS GINGIVALIS GENE DPP IV)"/CN OR
                 "DIPEPTIDYL PEPTIDASE IV (RAT)"/CN OR "DIPEPTIDYL PEPTIDASE IV
                 (STENOTROPHOMONAS MALTOPHILIA CLONE PXDP)"/CN OR "DIPEPTIDYL
                 PEPTIDASE IV (STREPTOCOCCUS GORDONII)"/CN OR "DIPEPTIDYL
                 PEPTIDASE IV (XENOPUS LAEVIS SKIN PRECURSOR)"/CN OR "DIPEPTIDYL
                  PEPTIDASE IV-RELATED PROTEIN (DEINOCOCCUS RADIODURANS STRAIN
                 R1 GENE DR2248)"/CN)
L12          173 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11(L)INHIBIT?
L13          103 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND L12
L14            9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 AND REVERS?
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                 OR TUMOR? OR ISCHEMIA? OR PARKINSON? OR MEMOR? OR HEARING? OR
                 VISION? OR MIGRAIN? OR BRAIN? OR SPINAL? OR ALZHEIMER? OR
                 AMYOTROPH? OR SCLEROS? OR DIABET? OR PROSTAT?)
L16           30 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15 NOT L14
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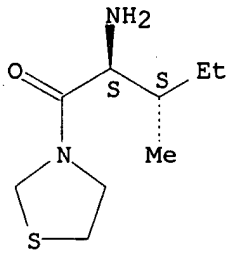
L14 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:880555 HCAPLUS
DN 136:160751
TI P32/98: Antidiabetic dipeptidyl-peptidase IV inhibitor
AU Sorbera, L. A.; Revel, L.; Castaner, J.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (2001), 26(9), 859-864
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
AB A review discusses the synthesis, pharmacol. actions, and clin. studies of P32/98, a novel class of antidiabetic agents. P32/98 is a highly specific, **reversible**, competitive, transition-state analog inhibitor of the regulatory enzyme, dipeptidyl peptidase IV that is involved in signal transduction processes occurring during the immune responses leading to development of type 2 diabetes. It has been chosen for further development as an agent having the potential to improve glucose tolerance and thus be advantageous in the management of type 2 diabetes.
IT **251572-86-8**, P 32/98
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(P 32/98; P32/98, an antidiabetic dipeptidyl-peptidase IV inhibitor, for treatment of type 2 diabetes in humans)
RN 251572-86-8 HCAPLUS
CN Thiazolidine, 3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (2E)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 136259-20-6
CMF C9 H18 N2 O S
CDES 1:S2:R*,R*

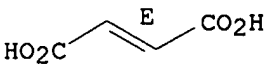
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

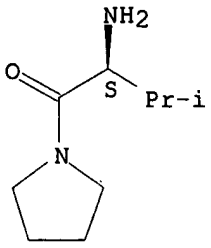


IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitor**; P32/98, an antidiabetic dipeptidyl-peptidase IV **inhibitor**, for treatment of type 2 diabetes in humans)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

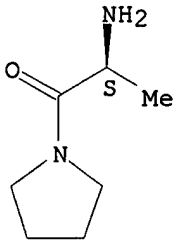
L14 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:868273 HCAPLUS
DN 134:189867
TI Potent inhibitors of dipeptidyl peptidase IV and their mechanisms of inhibition
AU Stockel-Maschek, Angela; Stiebitz, Beate; Born, Ilona; Faust, Jurgen; Mogelin, Werner; Neubert, Klaus
CS Department of Biochemistry and Biotechnology, Institute of Biochemistry, Martin-Luther-University Halle-Wittenberg, Halle, 06120, Germany
SO Advances in Experimental Medicine and Biology (2000), 477, 117-123
CODEN: AEMBAP; ISSN: 0065-2598
PB Kluwer Academic/Plenum Publishers
DT Journal
LA English
AB Dipeptidyl peptidase IV (DP IV) is a proline-specific serine protease which cleaves Xaa-Pro-dipeptides from the N-terminus of longer peptides. A series of product analogous amino acid amides contg. different structure modifications like substitution of a ring atom, variation of the ring size and/or the introduction of a thioxo amide bond, phosphono amide bond or reduced amide bond were done to characterize these compds. as inhibitors of DP IV. These compds. are mostly classical **reversible** inhibitors of DP IV. In contrast amino acyl-2-cyanopyrrolidides inhibit DP IV according to a slow-binding mechanism with inhibition consts. in the nanomolar range. On the other hand, diaryl dipeptide phosphonates inhibit irreversibly. In conclusion, this work shows, that the mechanism of inhibition of DP IV depends on the structure of the investigated compds.
IT **54164-07-7 56384-04-4 136259-18-2**
136259-19-3 136259-20-6 136259-21-7
136259-22-8 136259-23-9 171093-88-2
184360-52-9 184360-54-1 184360-55-2
184360-57-4 184360-58-5 252860-57-4
327623-45-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(potent inhibitors of dipeptidyl peptidase IV and their mechanisms of inhibition)
RN 54164-07-7 HCAPLUS
CN Pyrrolidine, 1-[(2S)-2-amino-3-methyl-1-oxobutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



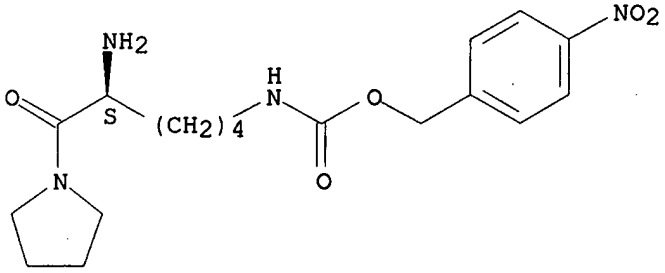
RN 56384-04-4 HCAPLUS
CN Pyrrolidine, 1-[(2S)-2-amino-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



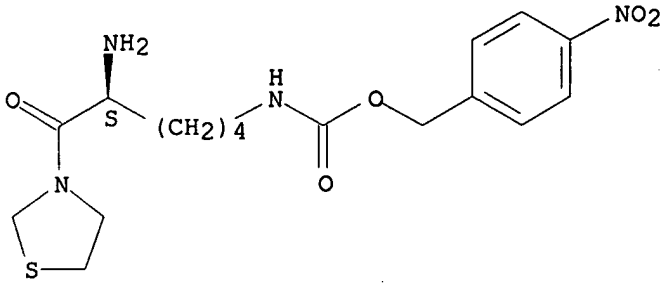
RN 136259-18-2 HCAPLUS
CN Carbamic acid, [(5S)-5-amino-6-oxo-6-(1-pyrrolidinyl)hexyl]-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



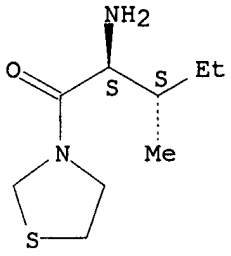
RN 136259-19-3 HCAPLUS
CN Carbamic acid, [(5S)-5-amino-6-oxo-6-(3-thiazolidinyl)hexyl]-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



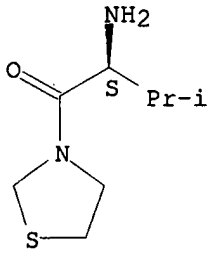
RN 136259-20-6 HCAPLUS
CN Thiazolidine, 3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



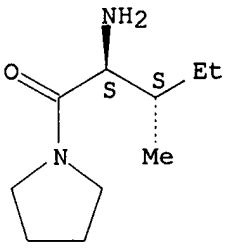
RN 136259-21-7 HCAPLUS
CN Thiazolidine, 3-[(2S)-2-amino-3-methyl-1-oxobutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



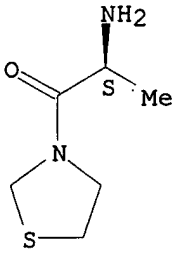
RN 136259-22-8 HCAPLUS
CN Pyrrolidine, 1-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



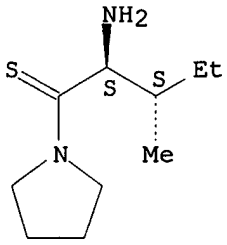
RN 136259-23-9 HCAPLUS
CN Thiazolidine, 3-[(2S)-2-amino-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



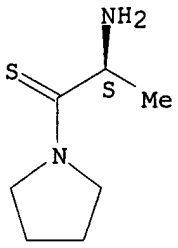
RN 171093-88-2 HCAPLUS
CN Pyrrolidine, 1-[(2S,3S)-2-amino-3-methyl-1-thioxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



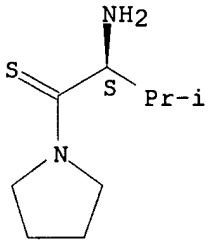
RN 184360-52-9 HCAPLUS
CN Pyrrolidine, 1-[(2S)-2-amino-1-thioxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



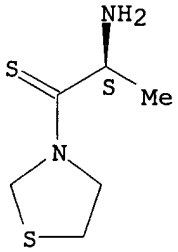
RN 184360-54-1 HCAPLUS
CN Pyrrolidine, 1-[(2S)-2-amino-3-methyl-1-thioxobutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



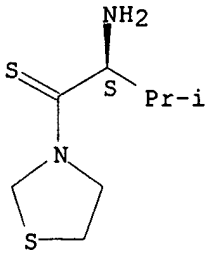
RN 184360-55-2 HCAPLUS
CN Thiazolidine, 3-[(2S)-2-amino-1-thioxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



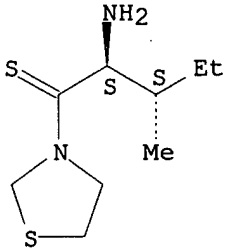
RN 184360-57-4 HCAPLUS
CN Thiazolidine, 3-[(2S)-2-amino-3-methyl-1-thioxobutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



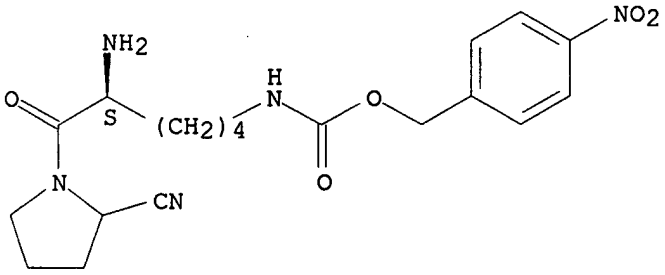
RN 184360-58-5 HCAPLUS
CN Thiazolidine, 3-[(2S,3S)-2-amino-3-methyl-1-thioxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



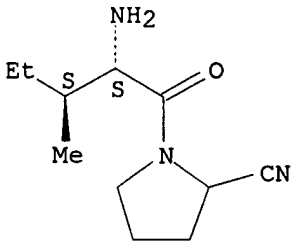
RN 252860-57-4 HCAPLUS
CN Carbamic acid, [(5S)-5-amino-6-(2-cyano-1-pyrrolidinyl)-6-oxohexyl]-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 327623-45-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(potent **inhibitors** of dipeptidyl peptidase IV and their mechanisms of **inhibition**)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

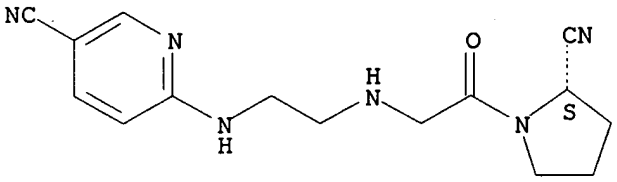
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:516472 HCAPLUS
DN 131:295099
TI NVP-DPP728 (1-[[[2-[(5-Cyanopyridin-2-yl)amino]ethyl]amino]acetyl]-2-cyano-(S)-pyrrolidine), a Slow-Binding Inhibitor of Dipeptidyl Peptidase IV
AU Hughes, Thomas E.; Mone, Manisha D.; Russell, Mary E.; Weldon, Stephen C.; Villhauer, Edwin B.
CS Metabolic and Cardiovascular Diseases Research, Novartis Institute for Biomedical Research, Summit, NJ, 07901-1398, USA
SO Biochemistry (1999), 38(36), 11597-11603
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
AB Inhibition of dipeptidyl peptidase IV (DPP-IV) has been proposed recently as a therapeutic approach to the treatment of type 2 diabetes. N-Substituted-glycyl-2-cyanopyrrolidide compds., typified by NVP-DPP728 (1-[[[2-[(5-cyanopyridin-2-yl)amino]ethyl]amino]acetyl]-2-cyano-(S)-pyrrolidine), inhibit degrdn. of glucagon-like peptide-1 (GLP-1) and thereby potentiate insulin release in response to glucose-contg. meals. In the present study NVP-DPP728 was found to inhibit human DPP-IV amidolytic activity with a Ki of 11 nM, a kon value of 1.3 .times. 105 M-1 s-1, and a koff of 1.3 .times. 10-3 s-1. Purified bovine kidney DPP-IV bound 1 mol/mol [14C]-NVP-DPP728 with high affinity (12 nM Kd). The dissocn. const., koff, was 1.0 .times. 10-3 and 1.6 .times. 10-3 s-1 in the presence of 0 and 200 .mu.M H-Gly-Pro-AMC, resp. (dissocn. t1/2 .apprx.10 min). Through kinetic evaluation of DPP-IV inhibition by the D-antipode, des-cyano, and amide analogs of NVP-DPP728, it was detd. that the nitrile functionality at the 2-pyrrolidine position is required, in the L-configuration, for maximal activity (Ki of 11 nM vs. Ki values of 5.6 to >300 .mu.M for the other analogs tested). Surprisingly, it was found that the D-antipode, despite being .apprx.500-fold less potent than NVP-DPP728, displayed identical dissocn. kinetics (koff of 1.5 .times. 10-3 s-1). NVP-DPP728 inhibited DPP-IV in a manner consistent with a

two-step inhibition mechanism. Taken together, these data suggest that NVP-DPP728 inhibits DPP-IV through formation of a novel, **reversible**, nitrile-dependent complex with transition state characteristics.

IT **247016-69-9**, NVP-DPP 728
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study)
(cyanopyrrolidide compd. NVP-DPP728 as slow-binding inhibitor of dipeptidyl peptidase IV)
RN 247016-69-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)amino]ethyl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

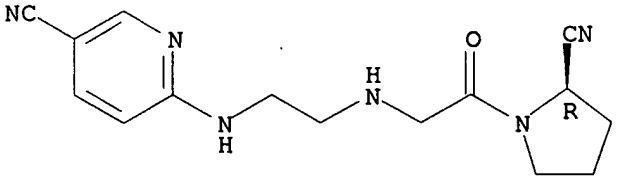
Absolute stereochemistry. Rotation (-).



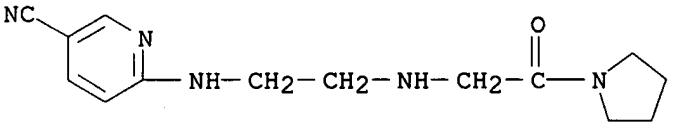
IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(cyanopyrrolidide compd. NVP-DPP728 as slow-binding **inhibitor** of dipeptidyl peptidase IV)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **246860-19-5 246860-20-8 246860-21-9**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study)
(inhibition of dipeptidyl peptidase IV by cyanopyrrolidide compd. NVP-DPP728 and analogs)
RN 246860-19-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)amino]ethyl]amino]acetyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

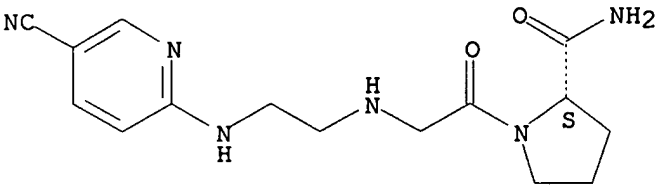


RN 246860-20-8 HCAPLUS
CN Pyrrolidine, 1-[[[2-[(5-cyano-2-pyridinyl)amino]ethyl]amino]acetyl]- (9CI) (CA INDEX NAME)



RN 246860-21-9 HCAPLUS
CN L-Prolinamide, N-[2-[(5-cyano-2-pyridinyl)amino]ethyl]glycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



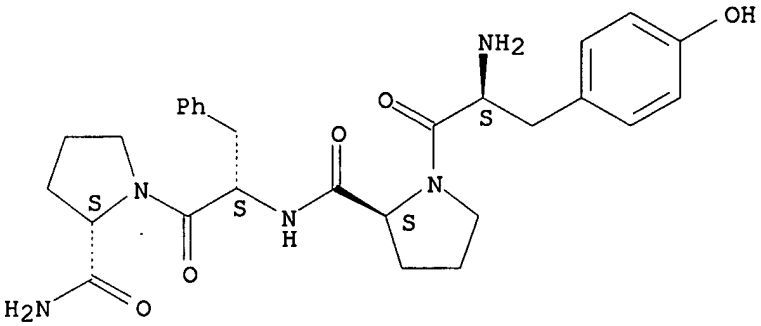
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:800993 HCAPLUS
DN 130:163108
TI Diprotin A, an inhibitor of dipeptidyl aminopeptidase IV(EC 3.4.14.5) produces naloxone-**reversible** analgesia in rats
AU Ronai, Andras Z.; Timar, Julianna; Mako, Eva; Erdo, Franciska; Gyarmati, Zsuzsanna; Toth, Geza; Orosz, Gyorgy; Furst, Susanne; Szekely, Jozsef I.
CS Department of Pharmacology, Semmelweis University of Medicine, Budapest, H-1445, Hung.
SO Life Sci. (1998), Volume Date 1999, 64(2), 145-152
CODEN: LIFSAK; ISSN: 0024-3205
PB Elsevier Science Inc.
DT Journal
LA English
AB The dipeptidyl aminopeptidase IV (DP IV) inhibitor Diprotin A produces a full, dose-dependent, short-lasting and naloxone-**reversible** analgesia in the rat tail-flick test when given intracerebroventricularly, with an ED50 of 295 nmol/rat but it has no direct opioid agonist activity in the longitudinal muscle strip of guinea-pig ileum bioassay. Two of the potential DP IV substrates, morphiceptin and endomorphin 1, identified recently in bovine brain were also analgesic given by similar route. The action of endomorphin I was more potent (ED50 = 7.9 nmol/rat) and slightly but significantly more sustained than that of Diprotin A. Diprotin A neither potentiated nor prolonged the effect of a marginally analgesic dose of endomorphin 1. The distinct time course and the lack of potentiation indicate that in the analgesic effect of Diprotin A in rats the protection of a brain Tyr-Pro-peptide other than endomorphin 1 is involved.
IT **74135-04-9**, Morphiceptin **90614-48-5**, Diprotin A
189388-22-5, Endomorphin 1
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(inhibitor of dipeptidyl aminopeptidase IV(EC 3.4.14.5) Diprotin A produces naloxone-**reversible** analgesia in rats in relation to effect of morphiceptin and endomorphin 1)

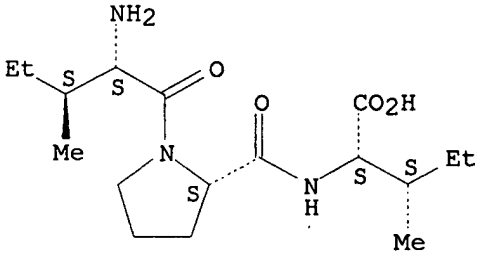
RN 74135-04-9 HCAPLUS
CN L-Prolinamide, L-tyrosyl-L-prolyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



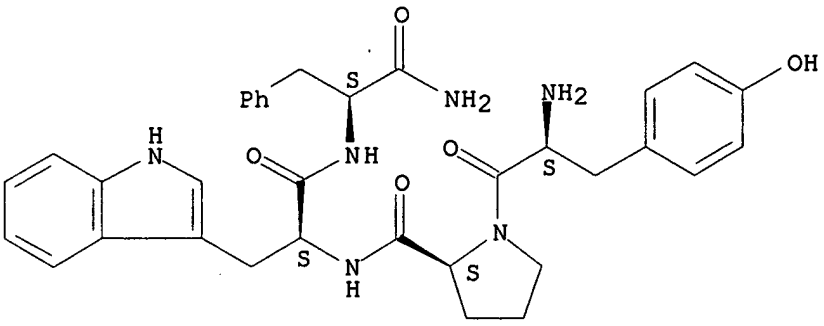
RN 90614-48-5 HCAPLUS
CN L-Isoleucine, L-isoleucyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 189388-22-5 HCAPLUS
CN L-Phenylalaninamide, L-tyrosyl-L-prolyl-L-tryptophyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



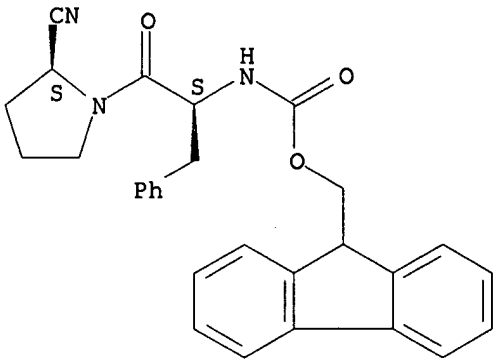
IT **54249-88-6**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitor** of dipeptidyl aminopeptidase IV(EC 3.4.14.5)
Diprotin A produces naloxone-**reversible** analgesia in rats in
relation to effect of morphiceptin and endomorphin 1)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

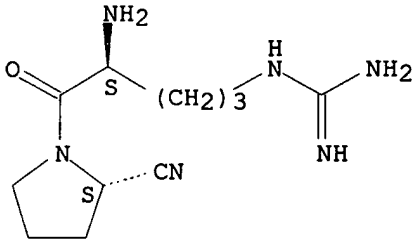
L14 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:660253 HCAPLUS
DN 127:314450
TI Inhibition of human immunodeficiency virus type 1 infection in a T-cell line (CEM) by new dipeptidyl-peptidase IV (CD26) inhibitors
AU Jiang, J. D.; Wilk, S.; Li, J.; Zhang, H.; Bekesi, J. G.
CS Division of Neoplastic Diseases of Department of Medicine, The Mount Sinai School of Medicine, New York, NY, 10029, USA
SO Res. Virol. (1997), 148(4), 255-266
CODEN: RESVEY; ISSN: 0923-2516
PB Elsevier
DT Journal
LA English
AB Phenylalanyl-pyrrolidine-2-nitrile (Phe-pyrr-2-CN) and arginyl(PMC)-pyrrolidine-2-nitrile (Arg(PMC)-pyrr-2-CN) are two dipeptidyl peptidase IV/CD26 (DPP-IV/CD26) inhibitors designed and synthesized by the authors group. These two compds. suppress the enzymic activity of DPP-IV/CD26 in a competitive and **reversible** manner. Pretreatment of CEM cells with either of the compds. yielded a marked albeit transient redn. of HIV infection, as measured by HIV1 p24 prodn., RT activity and syncytium formation. The ID50 value of Phe-Pyrr-2-CN and Arg(PMC)-pyrr-2-CN in HIV1 inhibition was 5.3 .mu.M and 2.4 .mu.M, resp. Administration of either of the DPP-IV/CD26 inhibitors 1 h after HIV1 infection did not suppress HIV1 prodn. An analog whose inhibitory activity toward DPP-IV/CD26 was abolished by blocking the N-terminal of Phe-pyrr-2-CN with the 9-fluorenymethyloxycarbonyl (Fmoc) group had no effect on HIV1 infection. An additive effect of HIV1 inhibition was obsd. in combinations of either of the DPP-IV/CD26 inhibitors with CD4 monoclonal antibody. These results suggest that DPP-IV/CD26 enzymic activity may play a role in facilitating HIV1 infection of human CD4+ T cells at the entry process. DPP-IV/CD26 inhibitors may therefore have potential use in combination with other drugs to prevent HIV1 transmission.
IT **169969-10-2 169969-15-7 169969-20-4**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of human immunodeficiency virus type 1 infection in a T-cell line (CEM) by new dipeptidyl-peptidase IV (CD26) inhibitors and their combination with CD4 monoclonal antibodies)
RN 169969-10-2 HCAPLUS
CN Carbamic acid, [2-(2-cyano-1-pyrrolidinyl)-2-oxo-1-(phenylmethyl)ethyl]-, 9H-fluoren-9-ylmethyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



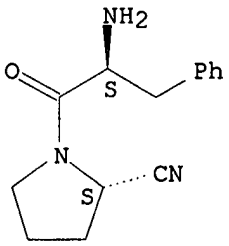
RN 169969-15-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[2-amino-5-[(aminoiminomethyl)amino]-1-oxopentyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 169969-20-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-(2-amino-1-oxo-3-phenylpropyl)-, [S-(R*,R*)]-(9CI) (CA INDEX NAME)

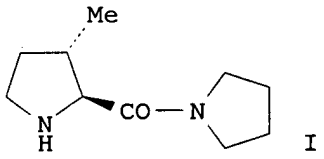
Absolute stereochemistry.



IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**inhibition** of human immunodeficiency virus type 1 infection in a T-cell line (CEM) by new dipeptidyl-peptidase IV (CD26) **inhibitors** and their combination with CD4 monoclonal antibodies)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L14 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:404876 HCAPLUS
DN 127:121976
TI Pyrrolidides: synthesis and structure-activity relationship as inhibitors of dipeptidyl peptidase IV
AU Augustyns, K.J.L.; Lambeir, A.M.; Borloo, M.; De Meester, I.; Vedernikova, I.; Vanhoof, G.; Hendriks, D.; Scharpe, S.; Haemers, A.
CS Department of Pharmaceutical Chemistry, University of Antwerp (UIA), Antwerp, B-2610, Belg.
SO Eur. J. Med. Chem. (1997), 32(4), 301-309
CODEN: EJMCA5; ISSN: 0223-5234
PB Elsevier
DT Journal
LA English
GI



I

AB Dipeptidyl peptidase IV cleaves specifically the peptide bond at the carboxyl side of a proline at the penultimate N-terminal position of a peptide. It is thought to be important for the regulation of biol. active peptides. Moreover, it has been identified as an activation marker of T-lymphocytes (CD26). Pyrrolidides and thiazolidides are known as **reversible** inhibitors of DPP IV. Several homologues, unsatd., open and 3-substituted analogs, e.g., I, were synthesized in order to det. the structure-activity relationship of the P-1 site. L-Isoleucine was taken as P-2 amino acid. 1-(L-Isoleucyl)-3(S)-fluoropyrrolidine is about as active as the non-fluorinated compd. and behaves as a competitive inhibitor. Other changes decrease or abolish the activity.

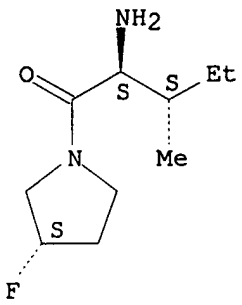
IT **175155-26-7P 192821-49-1P 192821-51-5P**
192821-53-7P 192821-55-9P 192821-57-1P
192821-59-3P 192821-60-6P 192821-70-8P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and structure activity of pyrrolidides as dipeptidyl peptidase IV inhibitors)

RN 175155-26-7 HCAPLUS
CN Pyrrolidine, 1-(2-amino-3-methyl-1-oxopentyl)-3-fluoro-, [3S-[1(2R*,3R*),3R*]]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

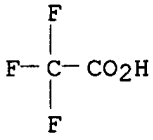
CRN 175155-25-6
CMF C10 H19 F N2 O
CDES *

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

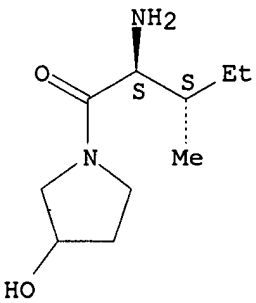


RN 192821-49-1 HCAPLUS
CN 3-Pyrrolidinol, 1-(2-amino-3-methyl-1-oxopentyl)-, [1(2S,3S)]-[partial]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 192821-48-0
CMF C10 H20 N2 O2

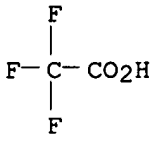
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2

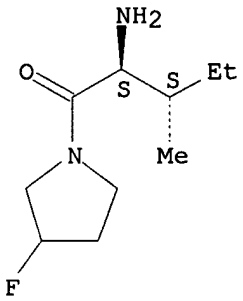


RN 192821-51-5 HCAPLUS
CN Pyrrolidine, 1-(2-amino-3-methyl-1-oxopentyl)-3-fluoro-, [1(2S,3S)]-[partial]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

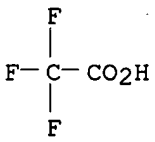
CRN 192821-50-4
CMF C10 H19 F N2 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

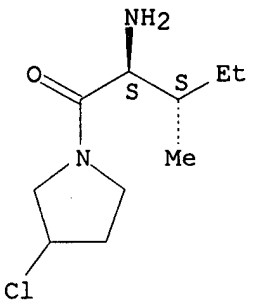


RN 192821-53-7 HCAPLUS
CN Pyrrolidine, 1-(2-amino-3-methyl-1-oxopentyl)-3-chloro-, [1(2S,3S)]-[partial]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

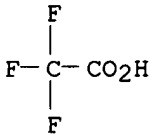
CRN 192821-52-6
CMF C10 H19 Cl N2 O

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

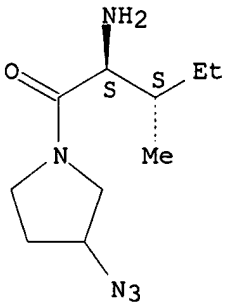


RN 192821-55-9 HCAPLUS
CN Pyrrolidine, 1-(2-amino-3-methyl-1-oxopentyl)-3-azido-, [1(2S,3S)]-[partial]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 192821-54-8
CMF C10 H19 N5 O

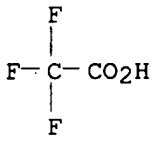
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2

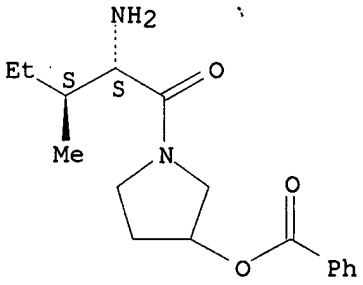


RN 192821-57-1 HCAPLUS
CN 3-Pyrrolidinol, 1-(2-amino-3-methyl-1-oxopentyl)-, benzoate (ester), [1(2S,3S)]-[partial]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

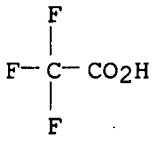
CRN 192821-56-0
CMF C17 H24 N2 O3

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

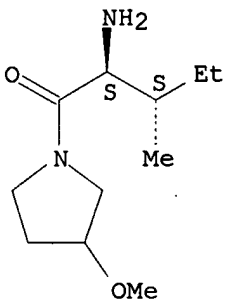


RN 192821-59-3 HCAPLUS
CN Pyrrolidine, 1-(2-amino-3-methyl-1-oxopentyl)-3-methoxy-, [1(2S,3S)]-[partial]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

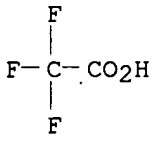
CRN 192821-58-2
CMF C11 H22 N2 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

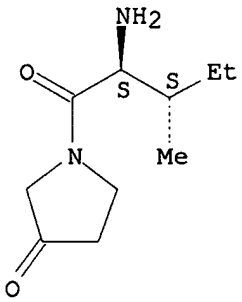


RN 192821-60-6 HCAPLUS
CN 3-Pyrrolidinone, 1-(2-amino-3-methyl-1-oxopentyl)-, [S-(R*,R*)]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

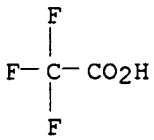
CRN 175155-40-5
CMF C10 H18 N2 O2
CDES 1:S2:R*,R*

Absolute stereochemistry.



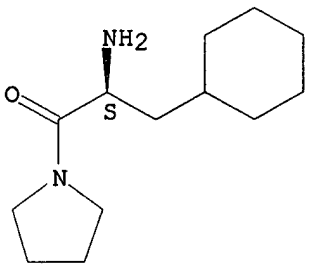
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 192821-70-8 HCAPLUS
CN Pyrrolidine, 1-(2-amino-3-cyclohexyl-1-oxopropyl)-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

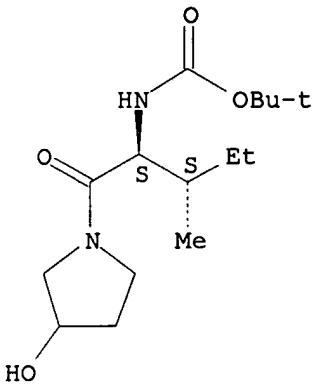


● HCl

IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prepn. and structure activity of pyrrolidides as dipeptidyl peptidase IV **inhibitors**)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

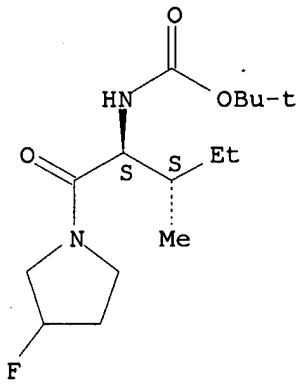
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **192821-47-9**
RL: RCT (Reactant)
(prepn. and structure activity of pyrrolidides as dipeptidyl peptidase IV inhibitors)
RN 192821-47-9 HCAPLUS
CN Carbamic acid, [1-[(3-hydroxy-1-pyrrolidinyl)carbonyl]-2-methylbutyl]-, 1,1-dimethylethyl ester, [1(1S,2S)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



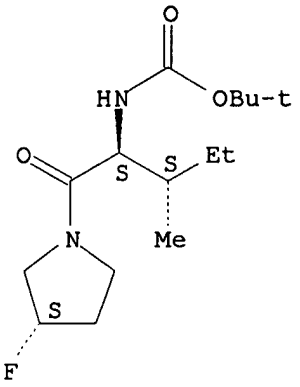
IT **192821-61-7P 192821-62-8P 192821-63-9P**
192821-64-0P 192821-65-1P 192821-66-2P
192821-67-3P 192821-68-4P 192821-69-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and structure activity of pyrrolidides as dipeptidyl peptidase IV inhibitors)
RN 192821-61-7 HCAPLUS
CN Carbamic acid, [1-[(3-fluoro-1-pyrrolidinyl)carbonyl]-2-methylbutyl]-, 1,1-dimethylethyl ester, [1(1S,2S)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



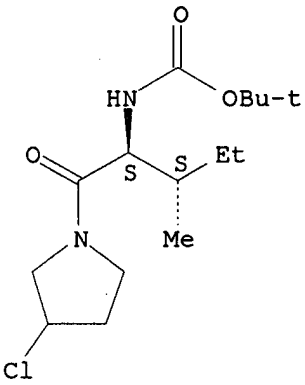
RN 192821-62-8 HCAPLUS
CN Carbamic acid, [1-[(3-fluoro-1-pyrrolidinyl)carbonyl]-2-methylbutyl]-, 1,1-dimethylethyl ester, [3S-[1(1R*,2R*),3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



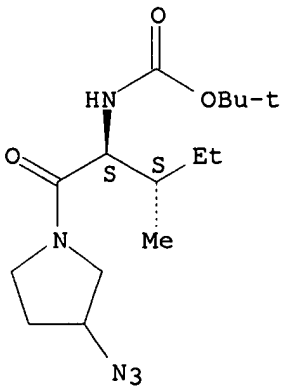
RN 192821-63-9 HCAPLUS
CN Carbamic acid, [1-[(3-chloro-1-pyrrolidinyl)carbonyl]-2-methylbutyl]-, 1,1-dimethylethyl ester, [1(1S,2S)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



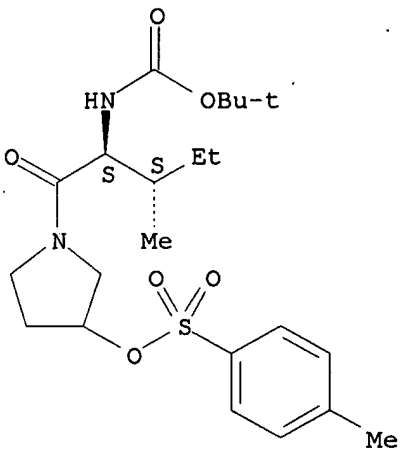
RN 192821-64-0 HCAPLUS
CN Carbamic acid, [1-[(3-azido-1-pyrrolidinyl)carbonyl]-2-methylbutyl]-, 1,1-dimethylethyl ester, [1(1S,2S)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



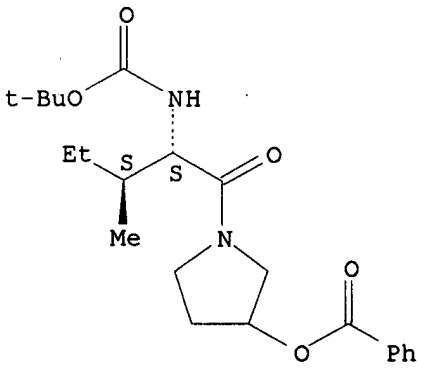
RN 192821-65-1 HCAPLUS
CN Carbamic acid, [2-methyl-1-[[3-[[(4-methylphenyl)sulfonyl]oxy]-1-pyrrolidinyl]carbonyl]butyl]-, 1,1-dimethylethyl ester, [1(1S,2S)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



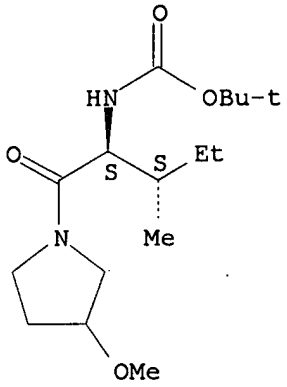
RN 192821-66-2 HCAPLUS
CN Carbamic acid, [1-[[3-(benzoyloxy)-1-pyrrolidinyl]carbonyl]-2-methylbutyl]-, 1,1-dimethylethyl ester, [1(1S,2S)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



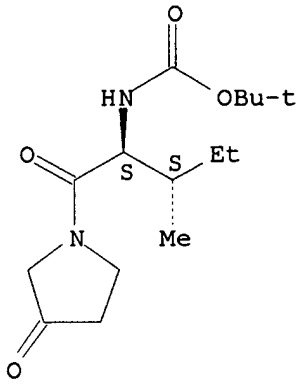
RN 192821-67-3 HCAPLUS
CN Carbamic acid, [1-[(3-methoxy-1-pyrrolidinyl)carbonyl]-2-methylbutyl]-, 1,1-dimethylethyl ester, [1(1S,2S)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



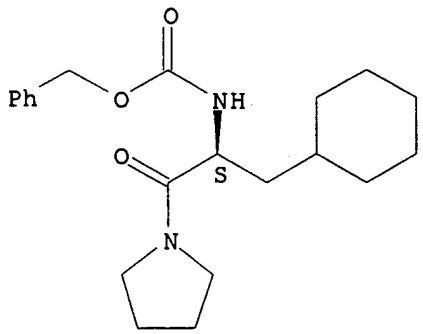
RN 192821-68-4 HCAPLUS
CN Carbamic acid, [2-methyl-1-[(3-oxo-1-pyrrolidinyl)carbonyl]butyl]-, 1,1-dimethylethyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

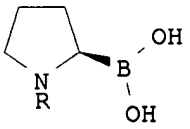


RN 192821-69-5 HCAPLUS
CN Carbamic acid, [1-(cyclohexylmethyl)-2-oxo-2-(1-pyrrolidinyl)ethyl]-, phenylmethyl ester, (S)- (9CI) (CA INDEX NAME)

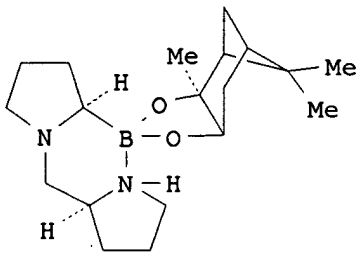
Absolute stereochemistry.



L14 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:183432 HCAPLUS
DN 122:240402
TI Studies on Proline Boronic Acid Dipeptide Inhibitors of Dipeptidyl Peptidase IV: Identification of a Cyclic Species Containing a B-N Bond
AU Snow, Roger J.; Bachovchin, William W.; Barton, Randall W.; Campbell, Scot J.; Coutts, Simon J.; Freeman, Dorothy M.; Gutheil, William G.; Kelly, Terence A.; Kennedy, Charles A.; et al.
CS Department of Medicinal Chemistry Pharmacology, Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, 06877, USA
SO J. Am. Chem. Soc. (1994), 116(24), 10860-9
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
GI



I



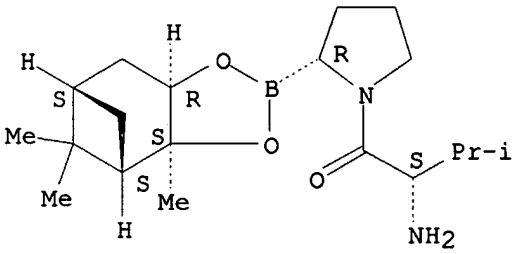
II

AB The proline boronic acid dipeptides I (R = H-Ala, H-Pro, H-Val) are very potent inhibitors of the enzyme dipeptidyl peptidase IV (DPP IV or CD26), found on the surface of T-cells, and are a new class of immunosuppressants. The efficient synthesis of the free boronic acids as single enantiomers is described, and the abs. configuration detd. I lose DPP IV inhibitory activity in soln.: this is shown to be due to the **reversible** formation of a cyclic species analogous to a diketopiperazine, contg. a B-N bond. The cyclic compds., both as the free boronic acids and as the pinanediol esters, were isolated and characterized by 1H and 11B NMR, and in the case of II, by x-ray crystallog. The cyclization is pH dependent, with the open form favored at low pH, while the cyclic form predominates at neutral pH. Both the rate and extent of cyclization depend on the N-terminal amino acid. The rates of cyclization have been measured by 1H NMR and shown to correlate with the decrease in DPP IV inhibitory activity. I (R = H-Val) cyclizes more slowly, and to a lesser extent than I (R = H-Ala, H-Pro), which is predicted to lead to greater immunosuppressive potency in vivo.
IT **162300-05-2P**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(crystal structure; prepn., cyclization, and dipeptidyl peptidase IV inhibitory activity of proline boronic acid dipeptides)
RN 162300-05-2 HCAPLUS
CN Pyrrolidine, 1-[(2S)-2-amino-3-methyl-1-oxobutyl]-2-[(3aS,4S,6S,7aR)-hexahydro-3a,5,5-trimethyl-4,6-methano-1,3,2-benzodioxaborol-2-yl]-, (2R)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 160332-26-3
CMF C19 H33 B N2 O3
CDES *

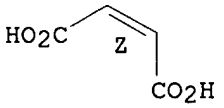
Absolute stereochemistry. Rotation (-).



CM 2

CRN 110-16-7
CMF C4 H4 O4
CDES 2:Z

Double bond geometry as shown.

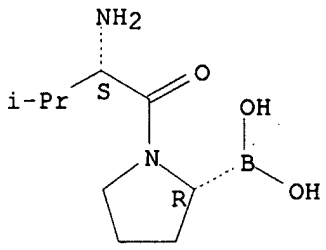


IT **150080-09-4P 162185-15-1P 162185-16-2P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn., cyclization, and dipeptidyl peptidase IV inhibitory activity of proline boronic acid dipeptides)
RN 150080-09-4 HCAPLUS
CN Boronic acid, [1-(2-amino-3-methyl-1-oxobutyl)-2-pyrrolidinyl]-, [R-(R*,S*)]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

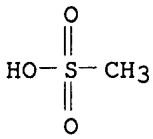
CRN 149682-77-9
CMF C9 H19 B N2 O3
CDES 1:R2:R*,S*

Absolute stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

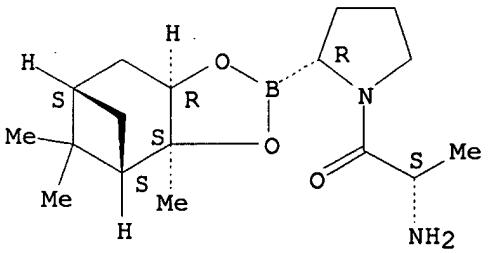


RN 162185-15-1 HCAPLUS
CN Pyrrolidine, 1-(2-amino-1-oxopropyl)-2-(hexahydro-3a,5,5-trimethyl-4,6-methano-1,3,2-benzodioxaborol-2-yl)-, [3aS-[2[S*(R*)],3a.alpha.,4.beta.,6.beta.,7a.alpha.]]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

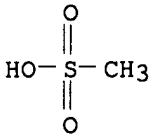
CRN 162185-14-0
CMF C17 H29 B N2 O3
CDES *

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-75-2
CMF C H4 O3 S

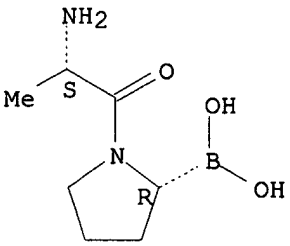


RN 162185-16-2 HCAPLUS
CN Boronic acid, [1-(2-amino-1-oxopropyl)-2-pyrrolidinyl]-, [R-(R*,S*)]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

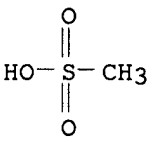
CRN 139649-82-4
CMF C7 H15 B N2 O3
CDES 1:R2:R*,S*

Absolute stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

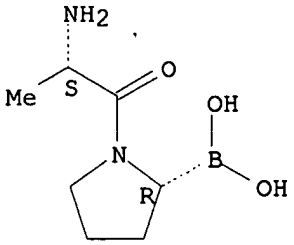


IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prepn., cyclization, and dipeptidyl peptidase IV **inhibitory** activity of proline boronic acid dipeptides)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **139649-82-4P 149682-77-9P 149716-75-6P**
160332-26-3P 162185-13-9P 162185-14-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn., cyclization, and dipeptidyl peptidase IV inhibitory activity of proline boronic acid dipeptides)

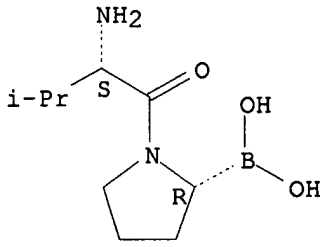
RN 139649-82-4 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-amino-1-oxopropyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



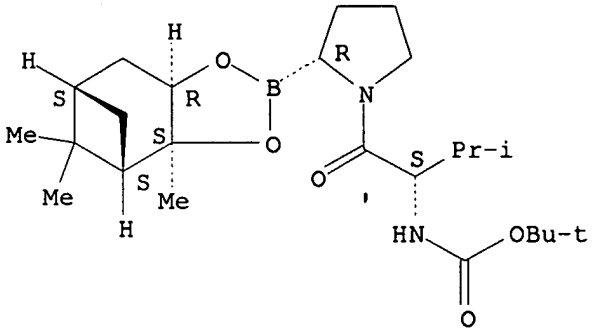
RN 149682-77-9 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-amino-3-methyl-1-oxobutyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 149716-75-6 HCAPLUS
CN Carbamic acid, [(1S)-1-[[(2R)-2-[(3aS,4S,6S,7aR)-hexahydro-3a,5,5-trimethyl-4,6-methano-1,3,2-benzodioxaborol-2-yl]-1-pyrrolidinyl]carbonyl]-2-methylpropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

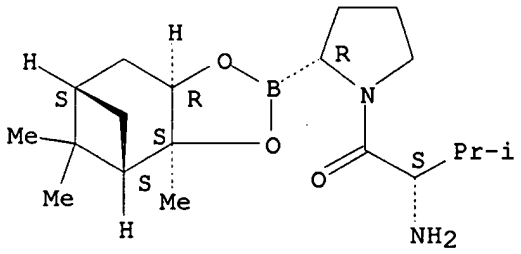
Absolute stereochemistry.



RN 160332-26-3 HCAPLUS
CN Pyrrolidine, 1-(2-amino-3-methyl-1-oxobutyl)-2-(hexahydro-3a,5,5-trimethyl-

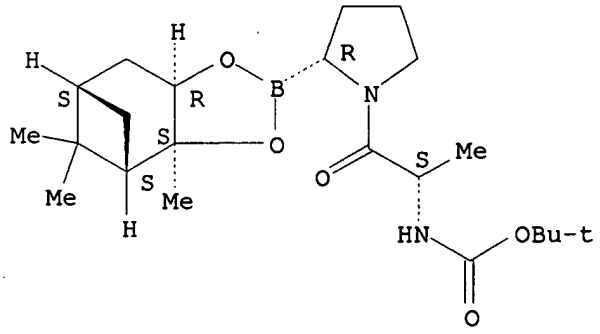
4,6-methano-1,3,2-benzodioxaborol-2-yl)-, [3aS-[2[S*(R*)],3a.alpha.,4.beta.,6.beta.,7a.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



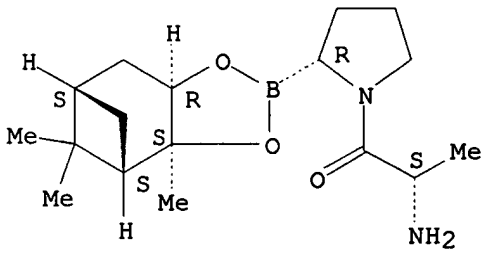
RN 162185-13-9 HCAPLUS
CN Carbamic acid, [2-[2-(hexahydro-3a,5,5-trimethyl-4,6-methano-1,3,2-benzodioxaborol-2-yl)-1-pyrrolidinyl]-1-methyl-2-oxoethyl]-, 1,1-dimethylethyl ester, [3aS-[2[S*(R*)],3a.alpha.,4.beta.,6.beta.,7a.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

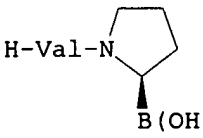


RN 162185-14-0 HCAPLUS
CN Pyrrolidine, 1-(2-amino-1-oxopropyl)-2-(hexahydro-3a,5,5-trimethyl-4,6-methano-1,3,2-benzodioxaborol-2-yl)-, [3aS-[2[S*(R*)],3a.alpha.,4.beta.,6.beta.,7a.alpha.]]- (9CI) (CA INDEX NAME)

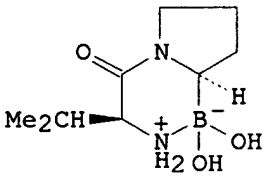
Absolute stereochemistry. Rotation (-).



L14 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:218507 HCAPLUS
DN 120:218507
TI Immunosuppresive boronic acid dipeptides: correlation between conformation and activity
AU Kelly, Terence A.; Adams, Julian; Bachovchin, William W.; Barton, Randall W.; Campbell, Scot J.; Coutts, Simon J.; Kennedy, Charles A.; Snow, Roger J.
CS Dep. Med. Chem., Boehringer Ingelheim Pharm. Inc., Ridgefield, CT, 06877, USA
SO J. Am. Chem. Soc. (1993), 115(26), 12637-8
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
GI



I

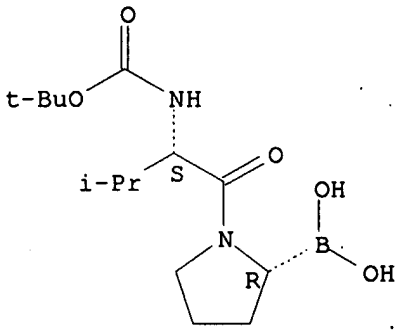


II

AB The correlation between the conformation and the immunosuppressive activity of the boronic acid-contg. dipeptide I was demonstrated. The rate of cyclization of I to II was measured by 1H-NMR techniques while the corresponding time-dependent loss of ability of the material to inhibit dipeptidyl peptidase IV was characterized via an enzyme assay. The rate consts. thus obtained point to II as being responsible for the deactivation of this inhibitor. Furthermore the **reversibility** of the cyclization was effected and showed to restore inhibitory activity against the enzyme. The enzymic consequences of the ensuring equil. between active and inactive conformations is discussed.
IT **54249-88-6**, Dipeptidyl peptidase IV
RL: RCT (Reactant)
(conformation of boronic acid dipeptide **inhibitor** in relation to)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

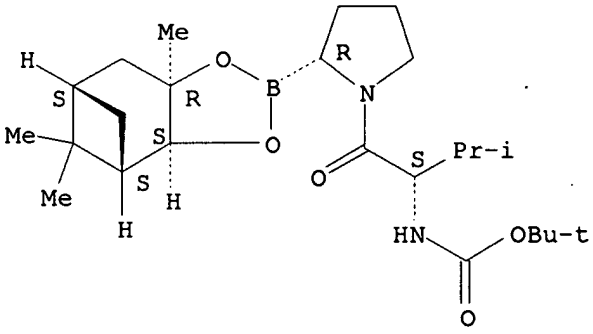
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **149682-78-0P 153760-44-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(intermediate in prepn. of boronic acid dipeptide)
RN 149682-78-0 HCAPLUS
CN Carbamic acid, [1-[(2-borono-1-pyrrolidinyl)carbonyl]-2-methylpropyl]-, C-(1,1-dimethylethyl) ester, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



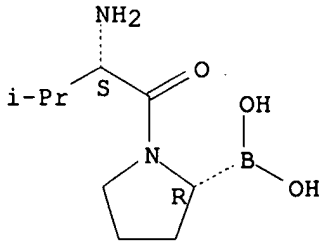
RN 153760-44-2 HCAPLUS
CN Carbamic acid, [1-[[2-(hexahydro-5,5,7a-trimethyl-4,6-methano-1,3,2-benzodioxaborol-2-yl)-1-pyrrolidinyl]carbonyl]-2-methylpropyl]-, 1,1-dimethylethyl ester, [3aS-[2[S*(R*)],3a.alpha.,4.beta.,6.beta.,7a.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **149682-77-9P 153737-95-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn., cyclization, and enzyme inhibitory activity of)
RN 149682-77-9 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-amino-3-methyl-1-oxobutyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

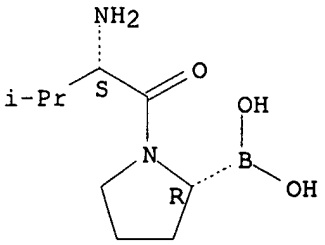
Absolute stereochemistry.



RN 153737-95-2 HCAPLUS

CN Boronic acid, [(2R)-1-[(2S)-2-amino-3-methyl-1-oxobutyl]-2-pyrrolidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L14 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:534096 HCAPLUS
DN 119:134096
TI Design of (.omega.-N-(O-acyl)hydroxyamido)aminodicarboxylic acid pyrrolidides as potent inhibitors of proline-specific peptidases
AU Demuth, H. U.; Schlenzig, D.; Schierhorn, A.; Grosche, G.; Chapot-Chartier, M. P.; Gripon, J. C.
CS Dep. Biochem., Martin-Luther-Univ., Halle/Saale, Germany
SO FEBS Lett. (1993), 320(1), 23-7
CODEN: FEBLAL; ISSN: 0014-5793
DT Journal
LA English
AB A novel class of competitive, acylating inhibitors for the proline-specific peptidases dipeptidyl peptidase IV, dipeptidyl peptidase II and prolyl endopeptidase, has been developed. The inhibitor mols. combine the efficacy of aminoacyl pyrrolidides and the potential transacylating capability of diacyl hydroxylamines. The N-terminal deblocked inhibitors are potent **reversible** inhibitors of porcine kidney dipeptidyl peptidase IV and human placenta dipeptidyl peptidase II, exhibiting Ki values in the .mu.M range. Boc-protected (.omega.-N-hydroxyacylamido)aminodiacarboxylic acid pyrrolidides inhibit substrate hydrolysis by prolyl endopeptidases from different sources competitively reaching Ki values of 30 nM to 60 .mu.M. Addnl., .alpha.-N-Boc-(.omega.-N-hydroxy acetyl)glutaminyl pyrrolidide modifies human placenta prolyl endopeptidase in a time-dependent reaction.
IT **54249-88-6**, Dipeptidyl peptidase IV
RL: PROC (Process)
(**inhibition** of, by ((acyl)hydroxyamido)aminodicarboxylic acid pyrrolidides, kinetics of)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

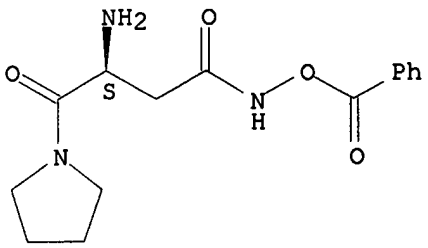
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **149575-36-0 149597-04-6 149597-05-7 149597-06-8 149597-07-9 149597-08-0 149798-60-7 149798-61-8**

RL: BIOL (Biological study)
(proline-specific peptidases inhibition by, kinetics of)

RN 149575-36-0 HCAPLUS

CN 1-Pyrrolidinebutanamide, .beta.-amino-N-(benzoyloxy)-.gamma.-oxo-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

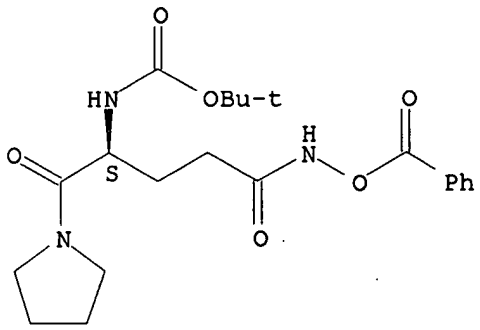


● HCl

RN 149597-04-6 HCAPLUS

CN Carbamic acid, [4-[(benzoyloxy)amino]-4-oxo-1-(1-pyrrolidinylcarbonyl)butyl]-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

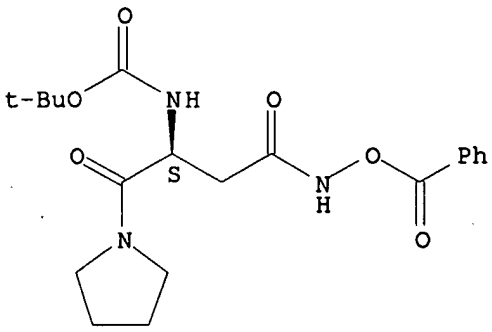
Absolute stereochemistry.



RN 149597-05-7 HCAPLUS

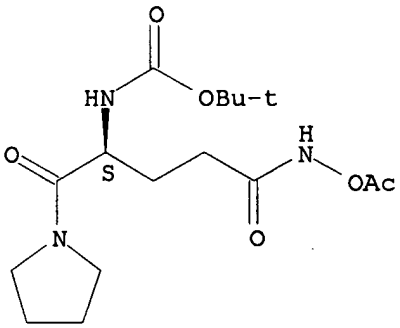
CN Carbamic acid, [3-[(benzoyloxy)amino]-3-oxo-1-(1-pyrrolidinylcarbonyl)propyl]-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



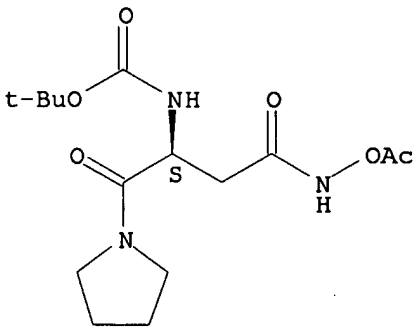
RN 149597-06-8 HCAPLUS
CN Carbamic acid, [4-[(acetyloxy)amino]-4-oxo-1-(1-pyrrolidinylcarbonyl)butyl]-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 149597-07-9 HCAPLUS
CN Carbamic acid, [3-[(acetyloxy)amino]-3-oxo-1-(1-pyrrolidinylcarbonyl)propyl]-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

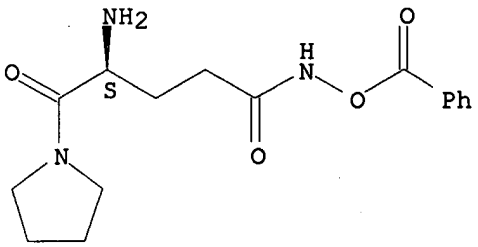
Absolute stereochemistry.



RN 149597-08-0 HCAPLUS

CN 1-Pyrrolidinepentanamide, .gamma.-amino-N-(benzoyloxy)-.delta.-oxo-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

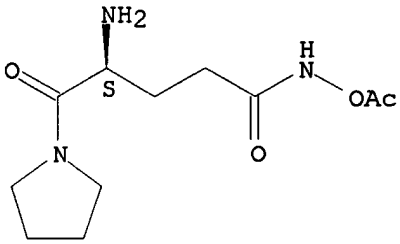
Absolute stereochemistry.



● HCl

RN 149798-60-7 HCAPLUS
CN 1-Pyrrolidinepentanamide, N-(acetyloxy)-.gamma.-amino-.delta.-oxo-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

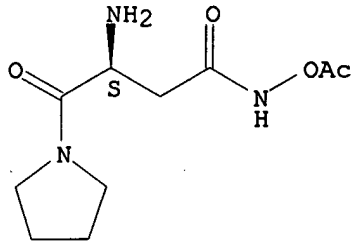
Absolute stereochemistry.



● HCl

RN 149798-61-8 HCAPLUS
CN 1-Pyrrolidinebutanamide, N-(acetyloxy)-.beta.-amino-.gamma.-oxo-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

INVENTOR SEARCH

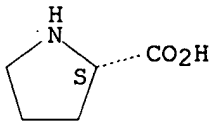
L5 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:359987 HCAPLUS
DN 134:348300
TI Dipeptidyl peptidase IV inhibitors and methods of making and using dipeptidyl peptidase IV inhibitors
IN **Jackson, Paul; Steiner, Joseph**
PA Guilford Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001034594	A1	20010517	WO 2000-US30836	20001113

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-439089 A 19991112
OS MARPAT 134:348300
AB Dipeptidyl peptidase IV inhibitors are provided which are based on or include proline or similar moieties. The inhibitors are useful for treating various disorders, including those of the central nervous system and the prostate. Many of the inhibitors can be reversible, and can cross the blood-brain barrier. Methods of making and using the inhibitors and treatment methods also are provided.
IT **147-85-3D**, L-Proline, mimetics, biological studies
54249-88-6, Dipeptidyl peptidase IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dipeptidyl peptidase IV inhibitors for therapeutic use)
RN 147-85-3 HCAPLUS
CN L-Proline (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 130:163108 CAPLUS
TI Diprotin A, an inhibitor of dipeptidyl aminopeptidase IV(EC 3.4.14.5) produces naloxone-reversible analgesia in rats
AU Ronai, Andras Z.; Timar, Julianna; Mako, Eva; Erdo, Franciska; Gyarmati, Zsuzsanna; Toth, Geza; Orosz, Gyorgy; Furst, Susanne; Szekely, Jozsef I.
CS Department of Pharmacology, Semmelweis University of Medicine, Budapest, H-1445, Hung.
SO Life Sciences (1998), Volume Date 1999, 64(2), 145-152
CODEN: LIFSAK; ISSN: 0024-3205
PB Elsevier Science Inc.
DT Journal
LA English
CC 1-11 (Pharmacology)
Section cross-reference(s): 2
AB The dipeptidyl aminopeptidase IV (DP IV) inhibitor Diprotin A produces a full, dose-dependent, short-lasting and naloxone-reversible analgesia in the rat tail-flick test when given intracerebroventricularly, with an ED50 of 295 nmol/rat but it has no direct opioid agonist activity in the longitudinal muscle strip of guinea-pig ileum bioassay. Two of the potential DP IV substrates, morphiceptin and endomorphin 1, identified recently in bovine brain were also analgesic given by similar route. The action of endomorphin I was more potent (ED50 = 7.9 nmol/rat) and slightly but significantly more sustained than that of Diprotin A. Diprotin A neither potentiated nor prolonged the effect of a marginally analgesic dose of endomorphin 1. The distinct time course and the lack of potentiation indicate that in the analgesic effect of Diprotin A in rats the protection of a brain Tyr-Pro-peptide other than endomorphin 1 is involved.
ST dipeptidyl aminopeptidase inhibitor Diprotin A analgesia
IT Analgesics
(inhibitor of dipeptidyl aminopeptidase IV(EC 3.4.14.5) Diprotin A produces naloxone-reversible analgesia in rats in relation to effect of morphiceptin and endomorphin 1)
IT 74135-04-9, Morphiceptin 90614-48-5, Diprotin A 189388-22-5, Endomorphin 1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor of dipeptidyl aminopeptidase IV(EC 3.4.14.5) Diprotin A produces naloxone-reversible analgesia in rats in relation to effect of morphiceptin and endomorphin 1)
IT 54249-88-6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor of dipeptidyl aminopeptidase IV(EC 3.4.14.5) Diprotin A produces naloxone-reversible analgesia in rats in relation to effect of morphiceptin and endomorphin 1)
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Arunlakshana, O; Br J Pharmacol 1959, V14, P48 CAPLUS
(2) Chang, K; Science 1981, V212, P75 CAPLUS
(3) Chipkin, R; Regulatory Peptides:From Molecular Biology to Function 1982
(4) Costentin, J; Eur J Pharmacol 1986, V123, P37 CAPLUS
(5) Endroczi, E; Acta Physiol Hung 1990, V73, P35
(6) Galina, Z; Life Science 1986, V39, P2153 CAPLUS
(7) Glass, G; Statistical methods in education and psychology 2nd ed 1984
(8) Graf, L; Nature 1976, V263, P240 CAPLUS
(9) Hackler, L; Peptides 1997, V18, P1635 CAPLUS
(10) Henscen, A; Endogenous and Exogenous Opiate Agonists and Antagonists 1980, P233
(11) Kosterlitz, H; Br J Pharmacol 1968, V33, P266 CAPLUS
(12) Leslie, F; Pharmacol Rew 1987, V39, P197 CAPLUS
(13) Litchfield, J; J Pharmacol Exp Ther 1949, V96, P99 CAPLUS
(14) Nyberg, F; .beta. - casomorphins and related peptides 1990

(15) Ronai, A; FEBS Lett 1977, V74, P182 CAPLUS
(16) Roques, B; Nature 1980, V288, P286 CAPLUS
(17) Schild, M; Peptides 1997, V18, P1641
(18) Snedecor, G; Statistical methods 8th ed, 5th printing 1994
(19) Szekely, J; Experientia 1977, V33, P54 CAPLUS
(20) Szekely, J; Opioid Peptides 1982, VII, P109
(21) Umezawa, H; J Antibiotics 1984, VXXXVII, P422
(22) Walter, R; Mol Cell Biochem 1980, V30, P111 CAPLUS
(23) Wood, P; Quo vadis? Analgesia & Enkephalinases 1984, P223 CAPLUS
(24) Yaksh, T; Eur J Pharmacol 1982, V79, P293 CAPLUS
(25) Zadina, J; Nature 1997, V386, P499 CAPLUS
(26) Zhang, A; Neuropharmacology 1982, V21, P625 CAPLUS

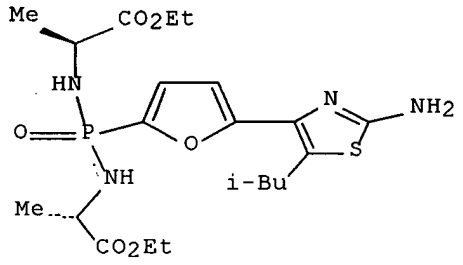
=>

L16 ANSWER 1 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:51257 HCAPLUS
DN 136:123595
TI A combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for the treatment of **diabetes**
IN Van Poelje, Paul D.; Erion, Mark D.; Fujiwara, Toshihiko
PA Metabasis Therapeutics, Inc., USA; Sankyo Company, Limited
SO PCT Int. Appl., 392 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

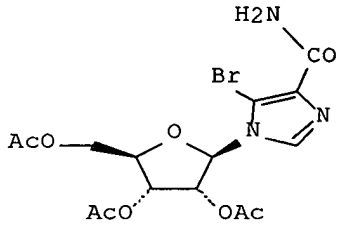
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002003978	A2	20020117	WO 2001-US21557	20010705

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-216531P P 20000706
OS MARPAT 136:123595
GI



I



II

AB A combination therapy of at least one FBPase inhibitor ((R1Y)2P(O)M and R14C(O)(CR12R13)nN(R18)P(O)(NR15R16)M; e.g. 2-amino-5-propylthio-4-(5-phosphono-2-furanyl)thiazole monohydrobromide and 2-amino-5-isobutyl-4-[2-[N,N'-bis[(S)-1-(ethoxycarbonyl)ethyl]phosphonodiamido]-5-furanyl]thiazole (shown as I)) and at least one other antidiabetic agent (insulin secretagogue; e.g. glyburide, a sulfonylurea) is disclosed. (R1Y)2P(O)M and R14C(O)(CR12R13)nN(R18)P(O)(NR15R16)M are converted in vivo or in vitro to MPO32-, which inhibit FBPase; the substituents are defined in the claims. General methods and about 15 specific example prepns. of the phosphorus compds. are included but no methods of prepn. are claimed. In the biol. examples, data is presented for the following for selected phosphorus compds. and other materials: inhibition of human liver FBPase, inhibition of rat liver and mouse liver FBPase, inhibition of gluconeogenesis by an FBPase inhibitor in rat hepatocytes, inhibition of glucose prodn. and elevation of fructose-1,6-bisphosphate levels in rat hepatocytes treated with FBPase inhibitors, anal. of hepatic and plasma drug metabolite levels, blood glucose, and hepatic fructose

1,6-bisphosphate levels after administration of compd. A (shown as II) p.o. to normal fasted rats, anal. of hepatic and plasma drug levels after administration of compds. i.p. to normal fasted rats, oral bioavailability detn. of two compds. and oral glucose lowering activity of two compds. For insulin secretagogues: insulin release from pancreatic islets, glucose lowering in the fasted rat, i.v. glucose tolerance in the fasted rat, oral glucose tolerance in the Zucker **diabetic** fatty rat, insulin secretion in the rat, inhibition of KATP-channels in mouse pancreatic beta-cells, and sulfonylurea receptor binding. Also included are: inhibition of dipeptidyl peptidase IV (DPP-IV inhibitors), alpha-glucosidase assay, glycogen phosphorylase assay, assay of glucose 6-phosphatase inhibitors, glucagon antagonist assay, amylin agonist assay, fatty acid oxidn. inhibitor assay, glucose lowering in the db/db mouse (FBPase inhibitor), glucose lowering in the ZDF rat, acute combination treatment of an insulin secretagogue and an FBPase inhibitor in the ZDF rat, chronic combination treatment of an insulin secretagogue and an FBPase inhibitor in the ZDF rat, acute combination treatment of insulin and an FBPase inhibitor in db/db mice, beneficial effect of chronic combination treatment of insulin and an FBPase inhibitor in db/db mice, and beneficial effect of chronic combination treatment of insulin and an FBPase inhibitor in db/db Mice. Also included are: acute combination treatment of insulin and an FBPase inhibitor in the Goto-Kakizaki rat, acute combination treatment of a biguanide and an FBPase inhibitor in db/db mice, acute combination treatment of an alpha glucosidase inhibitor and an FBPase inhibitor in Goto-Kakizaki rats, acute combination treatment of a glycogen phosphorylase inhibitor and an FBPase inhibitor in db/db or ob/ob mice, acute combination treatment of a glucose-6-phosphatase inhibitor and an FBPase inhibitor in db/db or ob/ob mice, acute combination treatment of an FBPase inhibitor and an amylin agonist, chronic combination treatment of a fatty acid oxidn. inhibitor and an FBPase inhibitor in the streptozotocin-induced **diabetic** rat.

IT **54249-88-6**, Dipeptidyl peptidase-IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

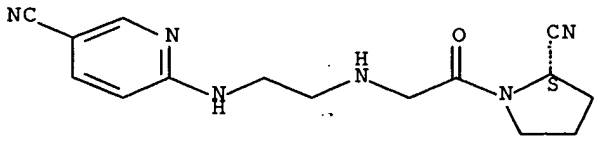
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

IT **247016-69-9**, NVP-DPP728 **251572-86-8**, P 32/98
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(insulin secretagogue; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of **diabetes**)

RN 247016-69-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)amino]ethyl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

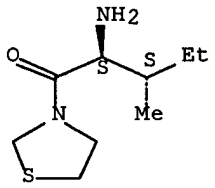


RN 251572-86-8 HCAPLUS
CN Thiazolidine, 3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (2E)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 136259-20-6
CMF C9 H18 N2 O S
CDES 1:S2:R*,R*

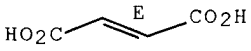
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



L16 ANSWER 2 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:935405 HCAPLUS
DN 136:48456
TI Combinations of depeptidyl peptidase IV inhibitors and other antidiabetic agents for the treatment of **diabetes** mellitus
IN Arch, Jonathan Robert Sanders; Lenhard, James Martin
PA Smithkline Beecham PLC, UK; Smithkline Beecham Corporation
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

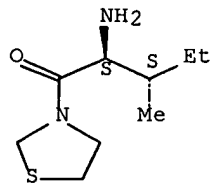
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001097808	A1	20011227	WO 2001-GB2696	20010619

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,

BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI GB 2000-14969 A 20000619
AB A method for the treatment of **diabetes** mellitus, esp. Type 2 **diabetes** and conditions assocd. with **diabetes** mellitus in a mammal, e.g. a human, comprises administering an effective, nontoxic and pharmaceutically acceptable amt. of a dipeptidyl peptidase IV inhibitor and another antidiabetic agent to a mammal in need thereof.
IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(depeptidyl peptidase IV **inhibitor** combination with other antidiabetic agent for treatment of **diabetes** mellitus)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

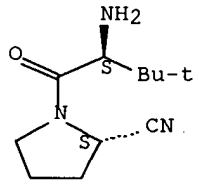
*** STRUCTURE DIAGRAM IS NOT AVAILABLE
IT **136259-20-6 171092-64-1 177931-21-4**
247016-69-9 251571-80-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(depeptidyl peptidase IV inhibitor combination with other antidiabetic agent for treatment of **diabetes** mellitus)
RN 136259-20-6 HCAPLUS
CN Thiazolidine, 3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



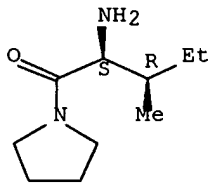
RN 171092-64-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-3,3-dimethyl-1-oxobutyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



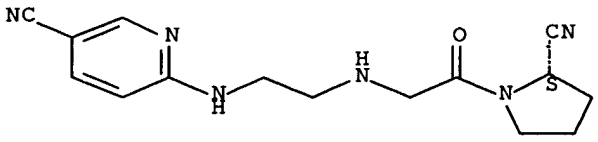
RN 177931-21-4 HCAPLUS
CN Pyrrolidine, 1-[(2S,3R)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



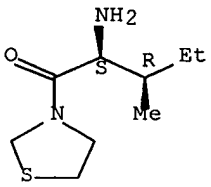
RN 247016-69-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)amino]ethyl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 251571-80-9 HCAPLUS
CN Thiazolidine, 3-[(2S,3R)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:923757 HCAPLUS
DN 136:37503
TI Preparation of N-glycyl-2-cyanopyrrolidines as DPP IV inhibitors
IN Villhauer, Edwin Bernard
PA Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001096295	A2	20011220	WO 2001-EP6595	20010611

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-592336 A 20000613

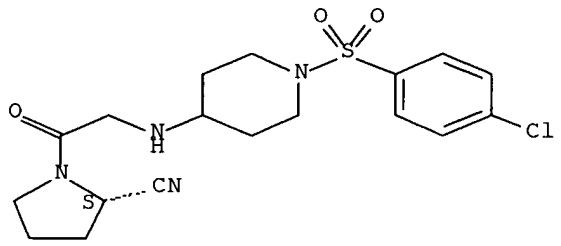
AB The present invention relates to the prepn. of N-(substituted glycyl)-2-cyanopyrrolidines. Thus, 1-chloroacetyl-2-(S)-cyanopyrrolidine (synthetic prepn. given) is reacted with 2-[(5-chloro-2-pyridinyl)amino]-1,1-dimethylethylamine in the presence of K2CO3 to give 1-[[[2-[(5-chloro-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-2-cyano-(S)-pyrrolidine. The prepd. compds. inhibit DPP-IV (dipeptidyl-peptidase-IV) activity. They are therefore indicated for use as pharmaceuticals in inhibiting DPP-IV and in the treatment of conditions mediated by DPP-IV, such as non-insulin-dependent **diabetes** mellitus, arthritis, obesity, osteoporosis and further conditions of impaired glucose tolerance. Data for biol. activity of some of the prepd. compds. were given.

IT **380829-08-3P**, 1-[[[1-[(4-Chlorophenyl)sulfonyl]-4-piperidinyl]amino]acetyl]-2-cyano-(S)-pyrrolidine
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(intermediate; prepn. of N-glycyl-2-cyanopyrrolidines as DPP IV inhibitors)

RN 380829-08-3 HCAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[1-[(4-chlorophenyl)sulfonyl]-4-piperidinyl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

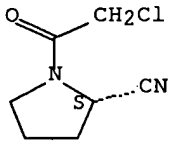


IT **207557-35-5P**, 1-Chloroacetyl-2-(S)-cyanopyrrolidine
380829-06-1P, 1-[[[1-(tert-Butoxycarbonylamino)-4-piperidinyl]amino]acetyl]-2-cyano-(S)-pyrrolidine **380829-07-2P**, 1-[[(4-Piperidinyl)amino]acetyl]-2-cyano-(S)-pyrrolidine dihydrochloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of N-glycyl-2-cyanopyrrolidines as DPP IV inhibitors)

RN 207557-35-5 HCAPLUS

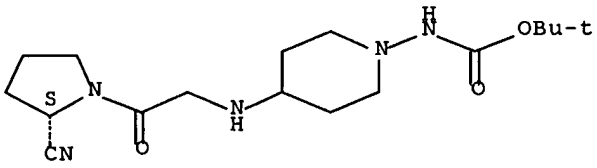
CN 2-Pyrrolidinecarbonitrile, 1-(chloroacetyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



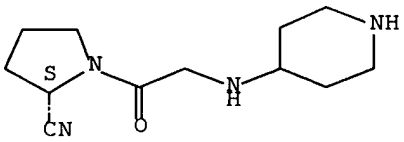
RN 380829-06-1 HCAPLUS
CN Carbamic acid, [4-[[2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxoethyl]amino]-1-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 380829-07-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[(4-piperidinylamino)acetyl]-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

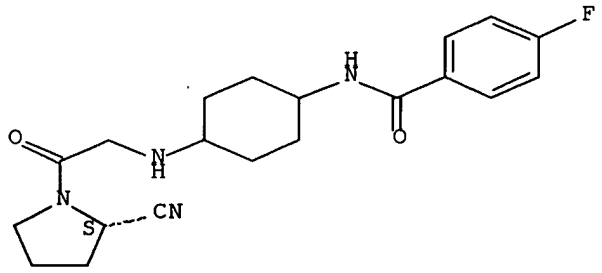


●2 HCl

IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mediated disorders, treatment; prepn. of N-glycyl-2-cyanopyrrolidines as DPP IV **inhibitors**)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
IT **380831-84-5P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of N-glycyl-2-cyanopyrrolidines as DPP IV inhibitors)
RN 380831-84-5 HCAPLUS
CN Benzamide, N-[4-[[2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxoethyl]amino]cyclohexyl]-4-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

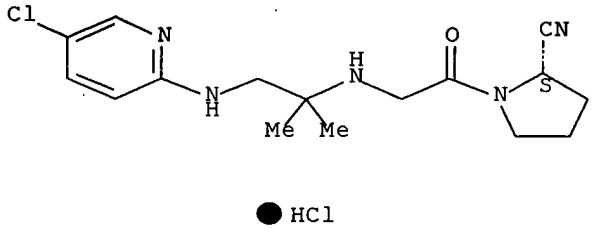


IT **380828-46-6P**, 1-[[[2-[(5-Chloro-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380828-85-3P**, 1-[[[2-[(5-Cyano-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-2-cyano-(S)-pyrrolidine **380828-86-4P**, 1-[[[2-[(5-Trifluoromethyl-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-2-cyano-(S)-pyrrolidine dihydrochloride **380828-87-5P**, 1-[[[2-[(4-Methylbenzoyl)amino]-1,1-dimethylethyl]amino]acetyl]-2-cyano-(S)-pyrrolidine **380828-88-6P**, 1-[[[2-[(3-Chloro-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-2-cyano-(S)-pyrrolidine dihydrochloride **380828-89-7P**, 1-[[[2-[(4-Trifluoromethyl-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-2-cyano-(S)-pyrrolidine **380828-90-0P**, 1-[[[2-[(3,5-Dichloro-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-2-cyano-(S)-pyrrolidine dihydrochloride **380828-91-1P**, 1-[[[2-[(3-Trifluoromethyl-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-2-cyano-(S)-pyrrolidine dihydrochloride **380828-92-2P**, 1-[[[2-[(2,2-Dimethyl-1-oxopropyl)amino]-1,1-dimethylethyl]amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380828-93-3P**, 1-[[[2-[(4-Chlorobenzoyl)amino]-1,1-dimethylethyl]amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380828-94-4P**, 1-[[[2-[[(Diisopropylamino)carbonyl]amino]-1,1-dimethylethyl]amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380828-95-5P**, 1-[[[2-[[[(4-Chlorophenyl)amino]carbonyl]amino]-1,1-dimethylethyl]amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380828-97-7P**, 1-[[2-[(4-Fluorophenyl)-1,1-dimethylethyl]amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380828-98-8P**, 1-[[(1,1-Dimethyl-2-phenylethyl)amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380828-99-9P**, 1-[[(4-Pentylbicyclo[2.2.2]oct-1-yl)amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380829-00-5P**, 1-[[[1-[[(4-Chlorophenyl)amino]carbonyl]-4-piperidinyl]amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380829-01-6P**, 1-[[[1-[(Diisopropylamino)carbonyl]-4-piperidinyl]amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380829-02-7P**, 1-[[[1-(4-Phenyl-2-thiazolyl)-4-piperidinyl]amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380829-03-8P**, 1-[[[1-[4-(4-Chlorophenyl)-2-thiazolyl)-4-piperidinyl]amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380829-04-9P**, 1-[[[1-[4-(4-Methoxyphenyl)-2-thiazolyl]-4-piperidinyl]amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380829-05-0P**, 1-[[[1-[(4-Chlorophenyl)sulfonyl]-4-piperidinyl]amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380829-09-4P**, 1-[[[1-(Cyclohexylcarbonyl)-4-piperidinyl]amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380829-10-7P**, 1-[[[1-(4-Chlorobenzoyl)-4-piperidinyl]amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380829-11-8P**, 1-[[[1-[[4-(Trifluoromethyl)phenyl]sulfonyl]-4-piperidinyl]amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380829-12-9P**,

1-[[(1-Phenylsulfonyl-4-piperidinyl)amino]acetyl]-2-cyano-(S)-pyrrolidine monohydrochloride **380831-62-9P 380831-63-0P**
380831-64-1P 380831-65-2P 380831-66-3P
380831-67-4P 380831-68-5P 380831-69-6P
380831-70-9P 380831-71-0P 380831-72-1P
380831-73-2P 380831-74-3P 380831-75-4P
380831-76-5P 380831-77-6P 380831-78-7P
380831-79-8P 380831-81-2P 380831-82-3P
380831-83-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-glycyl-2-cyanopyrrolidines as DPP IV inhibitors)

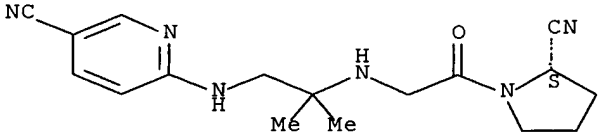
RN 380828-46-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-chloro-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-, monohydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



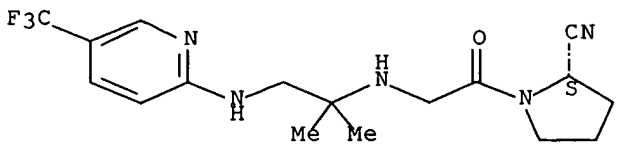
RN 380828-85-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 380828-86-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1,1-dimethyl-2-[[5-(trifluoromethyl)-2-pyridinyl]amino]ethyl]amino]acetyl]-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

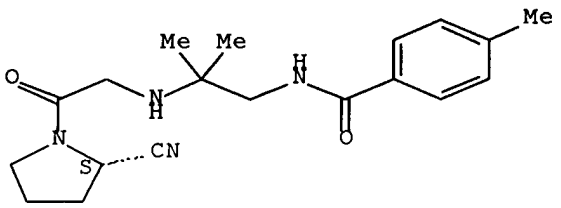
Absolute stereochemistry.



●2 HCl

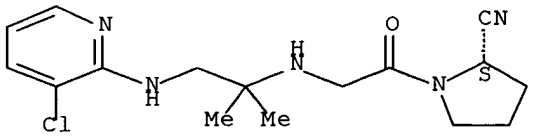
RN 380828-87-5 HCAPLUS
CN Benzamide, N-[2-[[2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxoethyl]amino]-2-methylpropyl]-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 380828-88-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(3-chloro-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

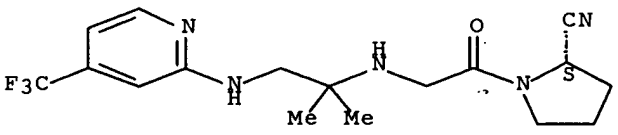
Absolute stereochemistry.



●2 HCl

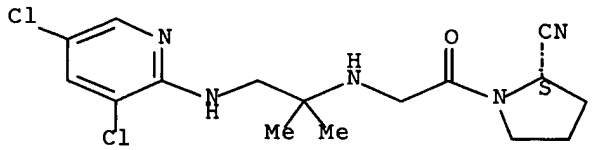
RN 380828-89-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1,1-dimethyl-2-[[4-(trifluoromethyl)-2-pyridinyl]amino]ethyl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 380828-90-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(3,5-dichloro-2-pyridinyl)amino]-1,1-dimethylethyl]amino]acetyl]-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

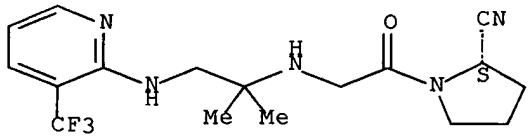
Absolute stereochemistry.



●2 HCl

RN 380828-91-1 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[1,1-dimethyl-2-[[3-(trifluoromethyl)-2-pyridinyl]amino]ethyl]amino]acetyl]-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

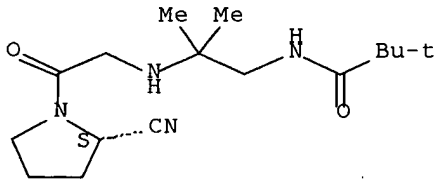
Absolute stereochemistry.



●2 HCl

RN 380828-92-2 HCAPLUS
CN Propanamide, N-[2-[[2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxoethyl]amino]-2-methylpropyl]-2,2-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)

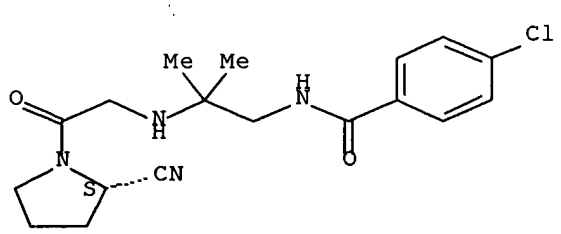
Absolute stereochemistry.



● HCl

RN 380828-93-3 HCAPLUS
CN Benzamide, 4-chloro-N-[2-[[2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxoethyl]amino]-2-methylpropyl]-, monohydrochloride (9CI) (CA INDEX NAME)

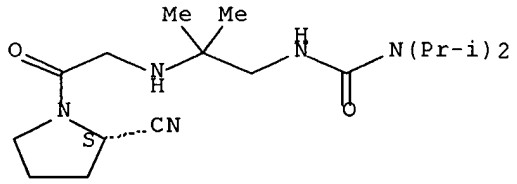
Absolute stereochemistry.



● HCl

RN 380828-94-4 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[[[bis(1-methylethyl)amino]carbonyl]amino]-1,1-dimethylethyl]amino]acetyl]-, monohydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L16 ANSWER 4 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:868260 HCAPLUS
DN 136:627
TI Combinations of enzyme inhibitor-containing preparations and the use in inhibition of mononuclear cells and T-cells and treatment of immune conditions
IN Ansorge, Siegfried; Arndt, Marco; Buehling, Frank; Lendeckel, Uwe; Neubert, Klaus; Reinhold, Dirk
PA Institut fuer Medizintechnologie Magdeburg G.m.b.H. IMTM, Germany
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001089569	A1	20011129	WO 2001-EP5887	20010522

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 10025464 A1 20011206 DE 2000-10025464 20000523

PRAI DE 2000-10025464 A 20000523

AB A method is disclosed which permits, owing to the simultaneous and joint inhibition of the enzyme activities of (1) alanyl-aminopeptidase and dipeptidyl-peptidase IV, (2) dipeptidyl-peptidase IV and angiotensin-converting enzyme, (3) dipeptidyl-peptidase IV and prolyl-oligopeptidase, and (4) dipeptidyl-peptidase IV and X-Pro-aminopeptidase, the inhibition of DNA synthesis and thus the proliferation of mononuclear cells and T cells to an extent which cannot be obtained by individual application of the enzyme inhibitors, even when used in higher doses. Although the above-mentioned inhibitors influence the same process, namely DNA synthesis and thus the proliferation of immune cells, this effect is not complete and not long-lasting when the inhibitors are used individually. The functional overlapping of enzymic activities results, as is supported by exptl. data, in an additive/superadditive inhibitory effect on DNA synthesis and the proliferation resulting from the simultaneous inhibition of a plurality of the above enzymes. The invention shows that the simultaneous application of inhibitors of the above enzymes or of corresponding prepns. and forms of administration is suitable for the therapy of autoimmune diseases and chronic diseases with an inflammatory genesis, as well as for the treatment of post-transplant rejection episodes.

IT **54249-88-6**, Dipeptidylpeptidase IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enzyme **inhibitor** combinations for **inhibition** of mononuclear cells and T-cells and treatment of immune conditions)

RN 54249-88-6 HCAPLUS

CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

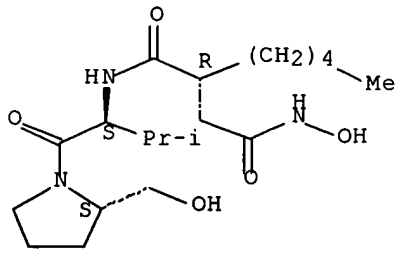
*** STRUCTURE DIAGRAM IS NOT AVAILABLE

IT **13434-13-4**, Actinonin **54164-07-7 56384-04-4**
62023-67-0 62571-86-2, Captopril **75847-73-3**,
Enalapril **76547-98-3**, Lisinopril **99429-59-1**
123652-87-9, Probestin **136259-18-2 136259-19-3**
136259-20-6 136259-21-7 136259-22-8
136259-23-9 160470-73-5, Apstatin **184360-42-7**
252860-56-3 252860-57-4 327623-45-0
327983-79-9 376346-22-4 376346-23-5
376346-24-6 376346-25-7 376346-26-8
376346-27-9
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enzyme inhibitor combinations for inhibition of mononuclear cells and T-cells and treatment of immune conditions)

RN 13434-13-4 HCAPLUS

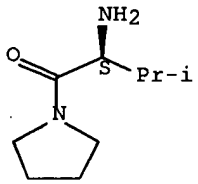
CN Butanediamide, N4-hydroxy-N1-[(1S)-1-[[(2S)-2-(hydroxymethyl)-1-pyrrolidinyl]carbonyl]-2-methylpropyl]-2-pentyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



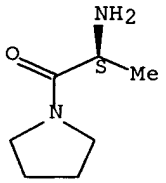
RN 54164-07-7 HCAPLUS
CN Pyrrolidine, 1-[(2S)-2-amino-3-methyl-1-oxobutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



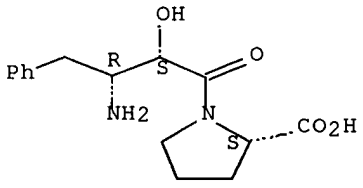
RN 56384-04-4 HCAPLUS
CN Pyrrolidine, 1-[(2S)-2-amino-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



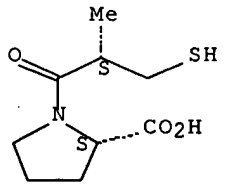
RN 62023-67-0 HCAPLUS
CN L-Proline, 1-[(2S,3R)-3-amino-2-hydroxy-1-oxo-4-phenylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



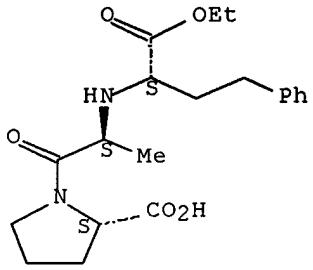
RN 62571-86-2 HCAPLUS
CN L-Proline, 1-[(2S)-3-mercapto-2-methyl-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



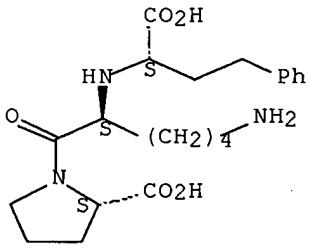
RN 75847-73-3 HCAPLUS
CN L-Proline, N-[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



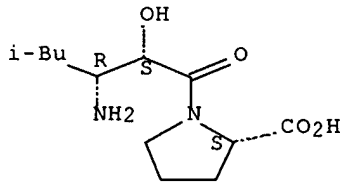
RN 76547-98-3 HCAPLUS
CN L-Proline, N2-[(1S)-1-carboxy-3-phenylpropyl]-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

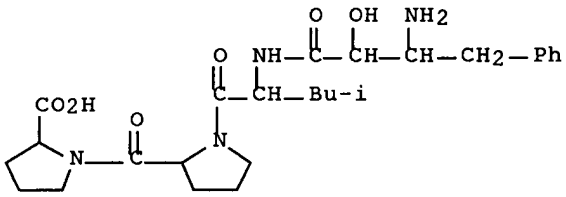


RN 99429-59-1 HCAPLUS
CN L-Proline, 1-[(2S,3R)-3-amino-2-hydroxy-5-methyl-1-oxohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

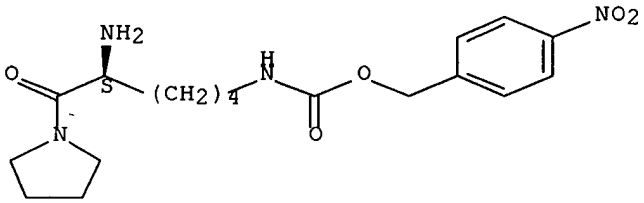


RN 123652-87-9 HCAPLUS
CN L-Proline, (.alpha.S,.beta.R)-.beta.-amino-.alpha.-hydroxybenzenebutanoyl-L-leucyl-L-prolyl- (9CI) (CA INDEX NAME)



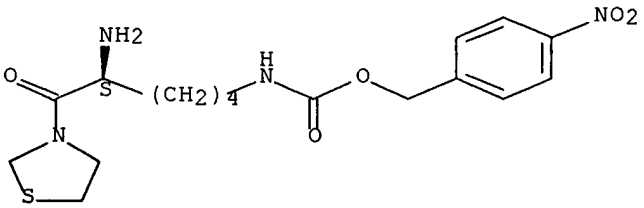
RN 136259-18-2 HCAPLUS
CN Carbamic acid, [(5S)-5-amino-6-oxo-6-(1-pyrrolidinyl)hexyl]-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



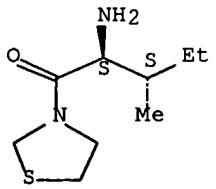
RN 136259-19-3 HCAPLUS
CN Carbamic acid, [(5S)-5-amino-6-oxo-6-(3-thiazolidinyl)hexyl]-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



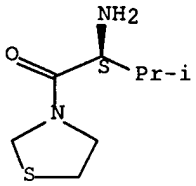
RN 136259-20-6 HCAPLUS
CN Thiazolidine, 3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



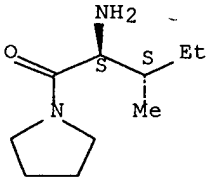
RN 136259-21-7 HCAPLUS
CN Thiazolidine, 3-[(2S)-2-amino-3-methyl-1-oxobutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



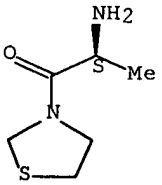
RN 136259-22-8 HCAPLUS
CN Pyrrolidine, 1-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



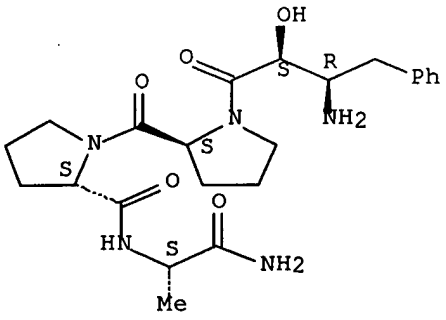
RN 136259-23-9 HCAPLUS
CN Thiazolidine, 3-[(2S)-2-amino-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



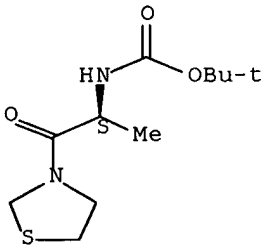
RN 160470-73-5 HCAPLUS
CN L-Alaninamide, 1-[(2S,3R)-3-amino-2-hydroxy-1-oxo-4-phenylbutyl]-L-prolyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



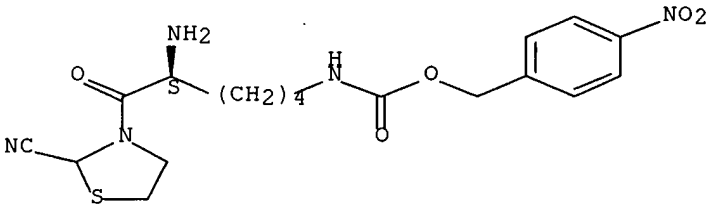
RN 184360-42-7 HCAPLUS
CN Carbamic acid, [(1S)-1-methyl-2-oxo-2-(3-thiazolidinyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



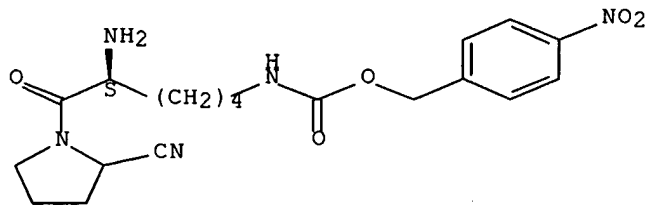
RN 252860-56-3 HCAPLUS
CN Carbamic acid, [(5S)-5-amino-6-(2-cyano-3-thiazolidinyl)-6-oxohexyl]-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 252860-57-4 HCAPLUS
CN Carbamic acid, [(5S)-5-amino-6-(2-cyano-1-pyrrolidinyl)-6-oxohexyl]-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

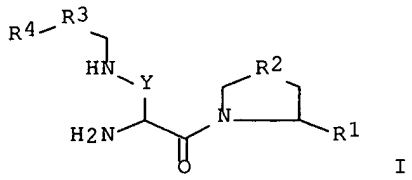


L16 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:798217 HCAPLUS
DN 135:344736
TI preparation of peptidomimetics as inhibitors of dipeptidyl peptidase IV
IN Evans, David Michael; Pitt, Gary Robert William
PA Ferring B.V., Neth.
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001081337	A1	20011101	WO 2001-GB1875	20010426

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2000-10188 A 20000426
OS MARPAT 135:344736
GI



I

AB Compds. of formula I [R1 = H or CN; R2 = S, O, SO2 or CH2; R3 = CO, CH2 or covalent bond; R4 = optionally substituted arom. N-contg. heterocycle; Y = (CH2)n; n = 1-5] were prepd. as inhibitors of dipeptidyl peptidase IV. Thus, compd. I (R1 = CN, R2 = H, R3 = CO, R4 = pyrazine, n = 3) was prepd. as trifluoroacetate via coupling of (2S)-pyrrolidine-2-carbonitrile hydrochloride (prepn. given) with N.alpha.-BOC-Nw-pyrazinyl-2-carbonyl-L-ornithine(BOC = tert-butoxycarbonyl). Compds. of the invention were competitive inhibitors of dipeptidyl peptidase IV with Ki values less than 300 nM.

IT **371241-16-6P 371241-20-2P 371241-22-4P**
371241-26-8P 371241-30-4P 371241-32-6P

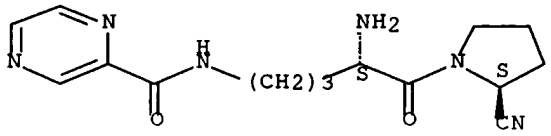
371241-33-7P 371241-34-8P 371241-37-1P
371241-39-3P 371241-41-7P 371241-44-0P
371241-48-4P 371241-51-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptidomimetics as inhibitors of dipeptidyl peptidase IV)

RN 371241-16-6 HCAPLUS
CN Pyrazinecarboxamide, N-[(4S)-4-amino-5-[(2S)-2-cyano-1-pyrrolidinyl]-5-oxopentyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

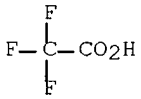
CRN 371241-15-5
CMF C15 H20 N6 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

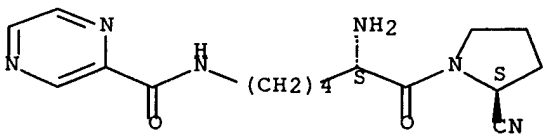


RN 371241-20-2 HCAPLUS
CN Pyrazinecarboxamide, N-[(5S)-5-amino-6-[(2S)-2-cyano-1-pyrrolidinyl]-6-oxohexyl]-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

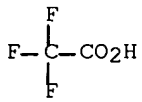
CRN 371241-19-9
CMF C16 H22 N6 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

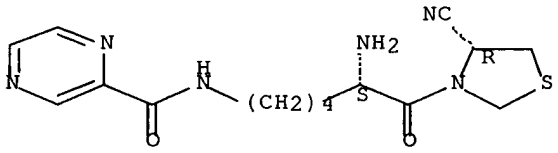


RN 371241-22-4 HCAPLUS
CN Pyrazinecarboxamide, N-[(5S)-5-amino-6-[(4R)-4-cyano-3-thiazolidinyl]-6-oxohexyl]-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

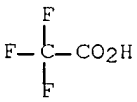
CRN 371241-21-3
CMF C15 H20 N6 O2 S

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

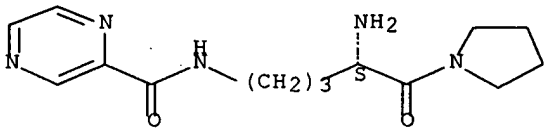


RN 371241-26-8 HCAPLUS
CN Pyrazinecarboxamide, N-[(4S)-4-amino-5-oxo-5-(1-pyrrolidinyl)pentyl]-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

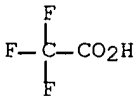
CRN 371241-25-7
CMF C14 H21 N5 O2

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

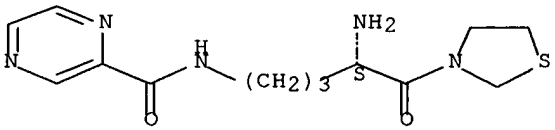


RN 371241-30-4 HCAPLUS
CN Pyrazinecarboxamide, N-[(4S)-4-amino-5-oxo-5-(3-thiazolidinyl)pentyl]-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

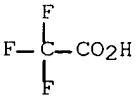
CRN 371241-29-1
CMF C13 H19 N5 O2 S

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

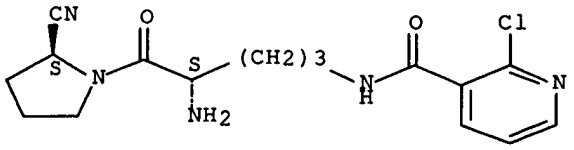


RN 371241-32-6 HCAPLUS
CN 3-Pyridinecarboxamide, N-[(4S)-4-amino-5-[(2S)-2-cyano-1-pyrrolidinyl]-5-oxopentyl]-2-chloro-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

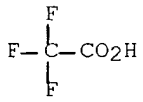
CRN 371241-31-5
CMF C16 H20 Cl N5 O2

Absolute stereochemistry.



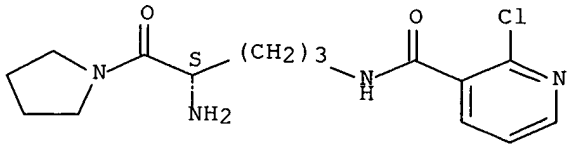
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 371241-33-7 HCAPLUS
CN 3-Pyridinecarboxamide, N-[(4S)-4-amino-5-oxo-5-(1-pyrrolidinyl)pentyl]-2-chloro-, hydrochloride (9CI) (CA INDEX NAME)

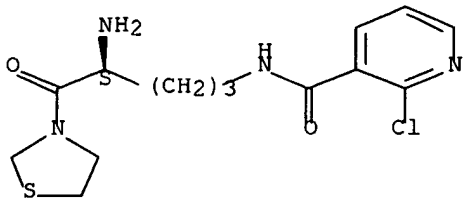
Absolute stereochemistry.



●x HCl

RN 371241-34-8 HCAPLUS
CN 3-Pyridinecarboxamide, N-[(4S)-4-amino-5-oxo-5-(3-thiazolidinyl)pentyl]-2-chloro-, hydrochloride (9CI) (CA INDEX NAME)

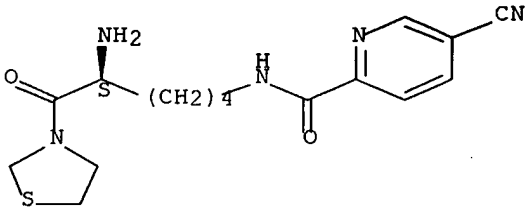
Absolute stereochemistry.



x HCl

RN 371241-37-1 HCAPLUS
CN 2-Pyridinecarboxamide, N-[(5S)-5-amino-6-oxo-6-(3-thiazolidinyl)hexyl]-5-cyano-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



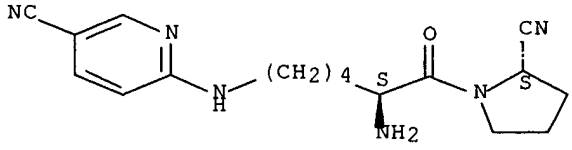
HCl

RN 371241-39-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[(2S)-2-amino-6-[(5-cyano-2-pyridinyl)amino]-1-oxohexyl]-, (2S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

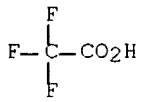
CRN 371241-38-2
CMF C17 H22 N6 O

Absolute stereochemistry.



CM 2

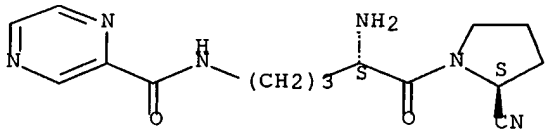
CRN 76-05-1
CMF C2 H F3 O2



IT **371241-15-5 371241-19-9 371241-21-3**
371241-25-7 371241-29-1 371241-31-5
371241-38-2 371241-40-6 371241-82-6
371241-83-7 371241-84-8 371241-85-9
371241-86-0 371241-87-1 371241-88-2
371241-89-3 371241-90-6 371241-91-7
371241-92-8 371241-93-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of peptidomimetics as inhibitors of dipeptidyl peptidase IV)

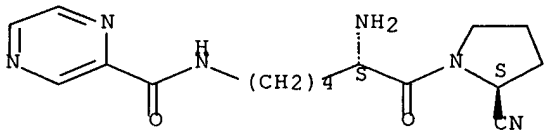
RN 371241-15-5 HCAPLUS
CN Pyrazinecarboxamide, N-[(4S)-4-amino-5-[(2S)-2-cyano-1-pyrrolidinyl]-5-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



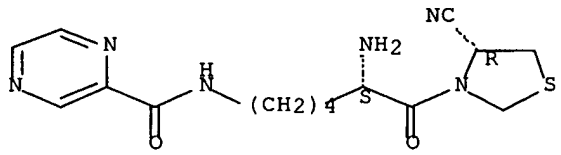
RN 371241-19-9 HCAPLUS
CN Pyrazinecarboxamide, N-[(5S)-5-amino-6-[(2S)-2-cyano-1-pyrrolidinyl]-6-oxohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



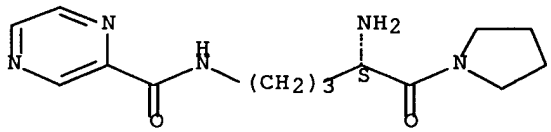
RN 371241-21-3 HCAPLUS
CN Pyrazinecarboxamide, N-[(5S)-5-amino-6-[(4R)-4-cyano-3-thiazolidinyl]-6-oxohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



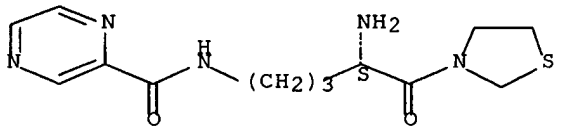
RN 371241-25-7 HCAPLUS
CN Pyrazinecarboxamide, N-[(4S)-4-amino-5-oxo-5-(1-pyrrolidinyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



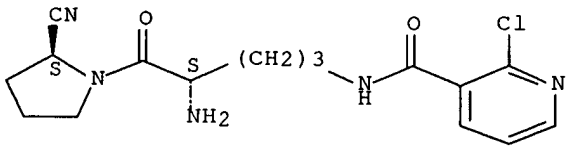
RN 371241-29-1 HCAPLUS
CN Pyrazinecarboxamide, N-[(4S)-4-amino-5-oxo-5-(3-thiazolidinyl)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 371241-31-5 HCAPLUS
CN 3-Pyridinecarboxamide, N-[(4S)-4-amino-5-[(2S)-2-cyano-1-pyrrolidinyl]-5-oxopentyl]-2-chloro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

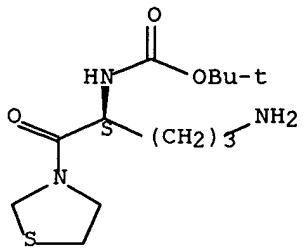


IT **371241-52-0P 371241-55-3P 371241-56-4P**
371241-57-5P 371241-58-6P 371241-60-0P
371241-62-2P 371241-63-3P 371241-64-4P
371241-65-5P 371241-66-6P 371241-67-7P
371241-68-8P 371241-69-9P 371241-70-2P
371241-71-3P 371241-72-4P 371241-73-5P
371241-74-6P 371241-75-7P 371241-76-8P

371241-77-9P 371241-78-0P 371241-79-1P
371241-80-4P 371241-81-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of peptidomimetics as inhibitors of dipeptidyl peptidase IV)

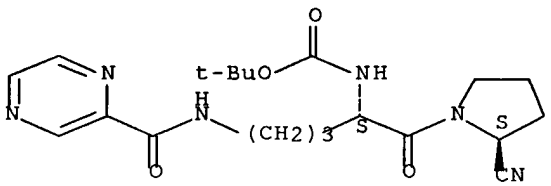
RN 371241-52-0 HCAPLUS
CN Carbamic acid, [(1S)-4-amino-1-(3-thiazolidinylcarbonyl)butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



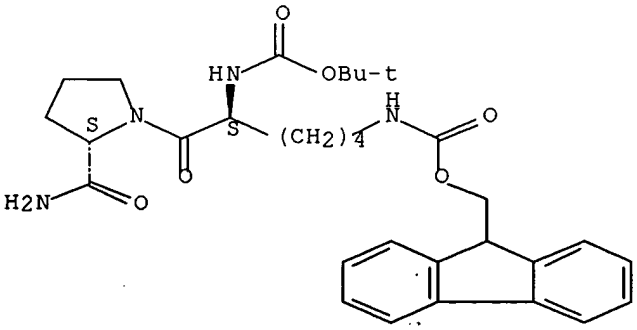
RN 371241-55-3 HCAPLUS
CN Carbamic acid, [(1S)-1-[[(2S)-2-cyano-1-pyrrolidinyl]carbonyl]-4-[(pyrazinylcarbonyl)amino]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



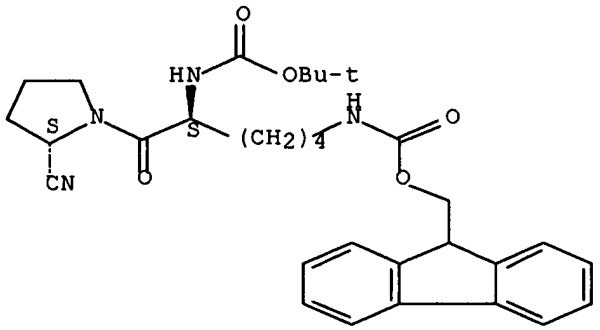
RN 371241-56-4 HCAPLUS
CN L-Prolinamide, N2-[(1,1-dimethylethoxy)carbonyl]-N6-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



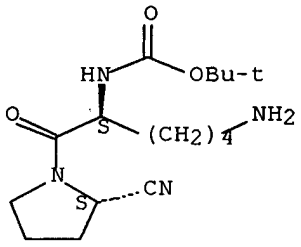
RN 371241-57-5 HCAPLUS
CN Carbamic acid, [(1S)-1-[[(2S)-2-cyano-1-pyrrolidinyl]carbonyl]-5-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]pentyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



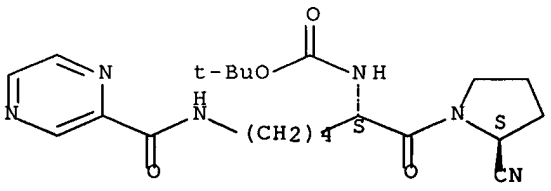
RN 371241-58-6 HCAPLUS
CN Carbamic acid, [(1S)-5-amino-1-[[(2S)-2-cyano-1-pyrrolidinyl]carbonyl]pentyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 371241-60-0 HCAPLUS
CN Carbamic acid, [(1S)-1-[[(2S)-2-cyano-1-pyrrolidinyl]carbonyl]-5-[(pyrazinylcarbonyl)amino]pentyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

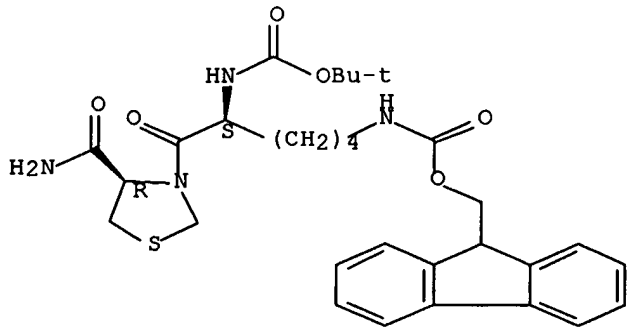
Absolute stereochemistry.



RN 371241-62-2 HCAPLUS
CN Carbamic acid, [(1S)-1-[[(4R)-4-(aminocarbonyl)-3-thiazolidinyl]carbonyl]-5-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]pentyl]-, 1,1-dimethylethyl

ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 6 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:730537 HCAPLUS
DN 135:267253
TI Method using dipeptidyl peptidase IV (DPIV) inhibitors for the improvement of islet signaling in **diabetes** mellitus and for its prevention
IN Demuth, Hans-Ulrich; Glund, Konrad
PA Probiodrug Gesellschaft Fuer Arzneimittelforschung MBH, Germany
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001072290	A2	20011004	WO 2001-EP3725	20010402
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2001051646	A1	20011213	US 2001-824622	20010402
PRAI	US 2000-194061P	P	20000331		

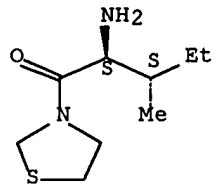
AB The invention discloses a method for therapeutically treating mammals, including but not limited to humans, to increase the relative insulin-producing performance of endogenous pancreatic .beta.-cells and to cause differentiation of pancreatic epithelial cells into insulin-producing .beta.-cells. Oral administration of a DPIV inhibitor causes the active form of GLP-1 to be preserved longer under physiol. conditions. The extended presence of GLP-1, in particular in the pancreatic tissue facilitates differentiation and regeneration of the .beta.-cells already present that are in need of repair. These repaired insulin-producing cells can contribute to the correction and maintenance of normal physiol. glycemic levels.

IT **136259-20-6 136259-22-8 177931-21-4**
251571-80-9 364041-91-8D, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(dipeptidyl peptidase IV inhibitors for improvement of islet signaling in **diabetes** mellitus and for **diabetes** prevention)

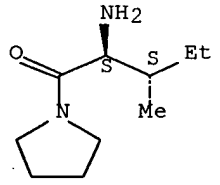
RN 136259-20-6 HCAPLUS
CN Thiazolidine, 3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



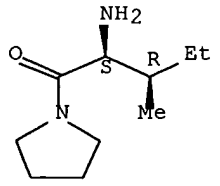
RN 136259-22-8 HCAPLUS
CN Pyrrolidine, 1-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



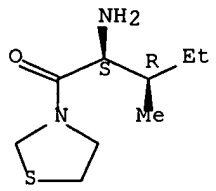
RN 177931-21-4 HCAPLUS
CN Pyrrolidine, 1-[(2S,3R)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

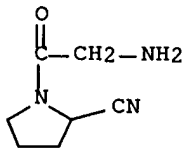


RN 251571-80-9 HCAPLUS
CN Thiazolidine, 3-[(2S,3R)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 364041-91-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-(aminoacetyl)- (9CI) (CA INDEX NAME)



IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dipeptidyl peptidase IV **inhibitors** for improvement of islet signaling in **diabetes** mellitus and for **diabetes** prevention)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

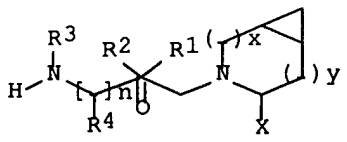
L16 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:693281 HCAPLUS
DN 135:257147
TI Preparation of fused cyclopropylpyrrolidine-based inhibitors of dipeptidyl peptidase IV
IN Robl, Jeffrey A.; Sulsky, Richard B.; Augeri, David J.; Magnin, David R.; Hamann, Lawrence G.; Betebenner, David A.
PA Bristol-Myers Squibb Co., USA
SO PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001068603	A2	20010920	WO 2001-US7151	20010305
WO 2001068603	A3	20020214		

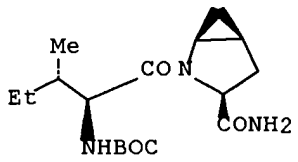
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002019411	A1	20020214	US 2001-788173	20010216

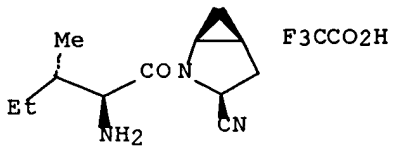
PRAI US 2000-188555P P 20000310
OS MARPAT 135:257147
GI



I



II



III

AB Dipeptidyl peptidase IV inhibiting compds. I (x = 0 or 1 and y = 0 or 1 provided that x = 1 when y = 0 and x = 0 when y = 1; n = 0, 1; X = H, CN; R1, R2, R3 and R4 = same or different and independently selected from H, (un)substituted chain or cyclic components) and the pharmaceutically acceptable salts or prodrugs (no data) were prepd. Thus L-pyroglutamic acid Et ester was protected, cyclopropanated and reacted further with (S)-N-BOC-isoleucine providing an intermediate II which reacted further to yield the fused cyclopropylpyrrolidine III in 57% yield. A method is also provided for treating **diabetes** and related diseases, esp. Type II **diabetes**, and other diseases by employing a title DP 4 inhibitor or a combination of DP 4 inhibitor and one or more of another antidiabetic agent such as metformin, glyburide, troglitazone, pioglitazone, rosiglitazone and/or insulin and/or one or more of a hypolipidemic agent and/or anti-obesity agent and/or other therapeutic agent.

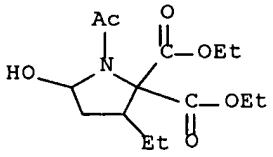
IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(prepn. of fused cyclopropylpyrrolidine-based **inhibitors** of dipeptidyl peptidase IV)

RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

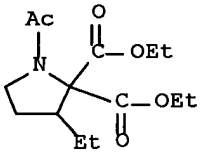
*** STRUCTURE DIAGRAM IS NOT AVAILABLE

IT **179015-57-7P 179015-58-8P 361442-26-4P 361442-27-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of fused cyclopropylpyrrolidine-based inhibitors of dipeptidyl peptidase IV)

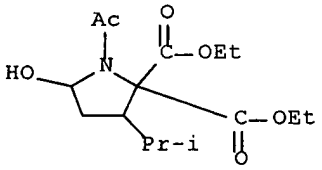
RN 179015-57-7 HCAPLUS
CN 2,2-Pyrrolidinedicarboxylic acid, 1-acetyl-3-ethyl-5-hydroxy-, diethyl ester (9CI) (CA INDEX NAME)



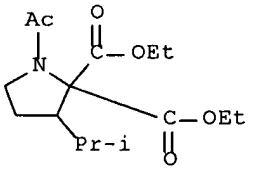
RN 179015-58-8 HCAPLUS
CN 2,2-Pyrrolidinedicarboxylic acid, 1-acetyl-3-ethyl-, diethyl ester (9CI) (CA INDEX NAME)



RN 361442-26-4 HCAPLUS
CN 2,2-Pyrrolidinedicarboxylic acid, 1-acetyl-5-hydroxy-3-(1-methylethyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 361442-27-5 HCAPLUS
CN 2,2-Pyrrolidinedicarboxylic acid, 1-acetyl-3-(1-methylethyl)-, diethyl ester (9CI) (CA INDEX NAME)



L16 ANSWER 8 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:635906 HCAPLUS
DN 135:190422
TI Inhibition of beta cell degeneration
IN Carr, Richard David
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 2

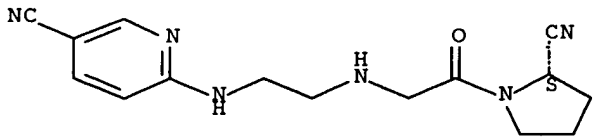
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001062266	A2	20010830	WO 2001-DK115	20010220
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	WO 2001055105	A1	20010802	WO 2001-DK45	20010122
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2001031780	A1	20011018	US 2001-767354	20010123
PRAI	DK 2000-295	A	20000225		
	DK 2000-983	A	20000623		
	WO 2001-DK45	W	20010122		
	DK 2000-112	A	20000124		
	US 2000-178856P	P	20000128		
	US 2000-216202P	P	20000706		

AB The present invention relates to a method preventing beta cell degeneration, such as necrosis or apoptosis of beta cells in a subject, comprising administering a DPP-IV (dipeptidyl peptidase IV) inhibitor to said subject. The invention furthermore relates to a method for increasing the no. and/or the size of beta cells. The invention also relates to a method for delaying the progression of Impaired Glucose Tolerance (IGT) to type 2 **diabetes**, as well as a method for delaying the progression of non-insulin demanding type 2 **diabetes** to insulin-demanding type 2 **diabetes**.

IT **247016-69-9**, NVP-DPP 728
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of beta cell degeneration using dipeptidyl peptidase IV inhibitors in relation to treatment of type 2 **diabetes** and combination with other agents)

RN 247016-69-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)amino]ethyl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **54249-88-6**, dipeptidyl peptidase IV
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**inhibition** of beta cell degeneration using dipeptidyl peptidase IV **inhibitors** in relation to treatment of type 2 **diabetes** and combination with other agents)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

L16 ANSWER 9 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:545464 HCAPLUS
DN 135:127207
TI Combinations comprising dipeptidylpeptidase-IV inhibitor
IN Balkan, Boerk; Hughes, Thomas Edward; Holmes, David Grenville; Villhauer, Edwin Bernard
PA Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001052825	A2	20010726	WO 2001-EP590	20010119

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-489234 A 20000121
US 2000-619262 A 20000719
OS MARPAT 135:127207
AB The invention relates to a combination which comprises a DPP-IV inhibitor and at least one further antidiabetic compd., preferably selected from the group consisting of insulin signalling pathway modulators, like inhibitors of protein tyrosine phosphatases (PTPases), non-small mol. mimetic compds. and inhibitors of glutamine-fructose-6-phosphate amidotransferase (GFAT), compds. influencing a dysregulated hepatic glucose prodn., like inhibitors of glucose-6-phosphatase (G6Pase), inhibitors of fructose-1,6-bisphosphatase (F-1,6-BPase), inhibitors of glycogen phosphorylase (GP), glucagon receptor antagonists and inhibitors of phosphoenolpyruvate carboxykinase (PEPCK), pyruvate dehydrogenase kinase (PDHK) inhibitors, insulin sensitivity enhancers, insulin secretion enhancers, .alpha.-glucosidase inhibitors, inhibitors of gastric emptying, insulin, and .alpha.2-adrenergic antagonists, for simultaneous, sep. or sequential use in the prevention, delay of progression or treatment of conditions mediated by dipeptidylpeptidase - IV (DPP-IV), in particular **diabetes**, more esp. type 2 **diabetes** mellitus, conditions of impaired glucose tolerance (IGT), conditions of impaired fasting plasma glucose, metabolic acidosis, ketosis, arthritis, obesity and osteoporosis;

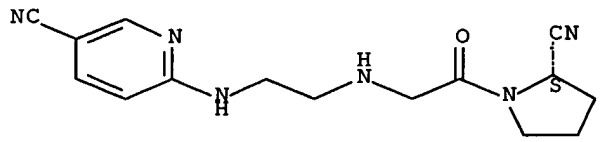
and the use of such combination for the cosmetic treatment of a mammal in order to effect a cosmetically beneficial loss of body wt. Tablets were prepd. contg. nateglinide.

IT **247016-69-9 274901-16-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations comprising dipeptidylpeptidase-IV inhibitor)

RN 247016-69-9 HCAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)amino]ethyl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

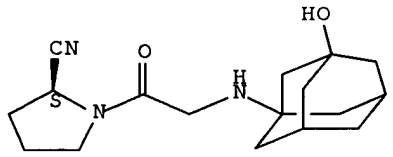
Absolute stereochemistry. Rotation (-).



RN 274901-16-5 HCAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **54249-88-6**, dipeptidylpeptidase-IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; combinations comprising dipeptidylpeptidase-IV **inhibitor**)

RN 54249-88-6 HCAPLUS

CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

L16 ANSWER 10 OF 30 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:283949 HCAPLUS

DN 134:311218

TI Synthesis and use of heterocyclic sodium/proton exchange inhibitors

IN Ahmad, Saleem; Wu, Shung C.; O'Neil, Steven V.; Ngu, Khehyong; Atwal, Karnail S.

PA Bristol-Myers Squibb Company, USA

SO PCT Int. Appl., 221 pp.
CODEN: PIXXD2

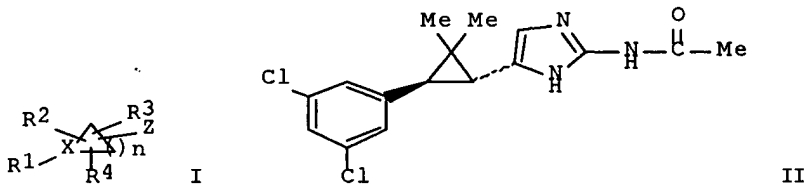
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001027107	A2	20010419	WO 2000-US27461	20001002

WO 2001027107 A3 20020124
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1999-158755P P 19991012
OS MARPAT 134:311218
GI



AB Compds. of formula I [wherein; n is 1-5; X is N or CR5, where R5 is H, halo, alkenyl, alkynyl, alkoxy, alkyl, aryl or heteroaryl; Z is a heteroaryl group; R1 is H, alk(en)(yn)yl, alk(enyl)(ynyl)oxy, (aryl or alkyl)3Si, cycloalk(en)yl, (aryl)amino, aryl(alkyl), cycloheteroaryl, etc.; R2, R3 and R4 are any of the groups set out for R1 and optionally substituted with 1 to 5 substituents which may be the same or different and when X is N, R1 is preferably aryl or heteroaryl] are claimed. Several hundred examples are disclosed. Synthesis of II proceeds via cyclopropanation of the cinnamate derived from the olefination between 3,5-dichlorobenzaldehyde and t-butyldiethylphosphonoacetate. The intermediate tert-Bu ester is converted to the corresponding .alpha.-chloroketone and reacted with acetyl guanidine to provide II in a total of 5 steps. Compds. I are said to be sodium/proton exchange inhibitors (NHE). Pharmaceutical combinations are claimed using I and certain antihypertensive agents, .beta.-adrenergic agonists, hypolipidemic agents, antidiabetic agents, antiobesity agents, etc. Compds. I are useful as antianginal and cardioprotective agents and provide a method for preventing or treating angina pectoris, cardiac dysfunction, myocardial necrosis, and arrhythmia.

IT **54249-88-6**, Dipeptidyl peptidase iv
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**inhibitor**, pharmaceuticals also contg.)

RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

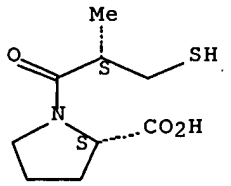
IT **62571-86-2**, Captopril **75847-73-3**, Enalapril **76547-98-3**, Lisinopril **80830-42-8**, Fentiapril **98048-97-6**, Fosinopril **251572-86-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceuticals also contg.; synthesis and use of heterocyclic sodium/proton exchange inhibitors)

RN 62571-86-2 HCAPLUS

CN L-Proline, 1-[(2S)-3-mercapto-2-methyl-1-oxopropyl]- (9CI) (CA INDEX NAME)

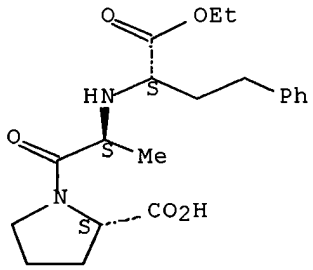
Absolute stereochemistry. Rotation (-).



RN 75847-73-3 HCAPLUS

CN L-Proline, N-[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]-L-alanyl- (9CI) (CA INDEX NAME)

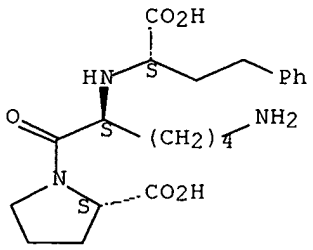
Absolute stereochemistry. Rotation (-).



RN 76547-98-3 HCAPLUS

CN L-Proline, N2-[(1S)-1-carboxy-3-phenylpropyl]-L-lysyl- (9CI) (CA INDEX NAME)

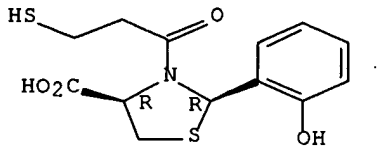
Absolute stereochemistry. Rotation (-).



RN 80830-42-8 HCAPLUS

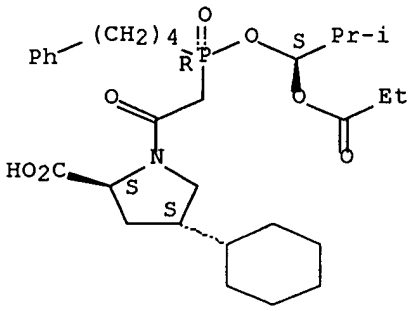
CN 4-Thiazolidinecarboxylic acid, 2-(2-hydroxyphenyl)-3-(3-mercapto-1-oxopropyl)-, (2R,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 98048-97-6 HCAPLUS
CN L-Proline, 4-cyclohexyl-1-[[(R)-[(1S)-2-methyl-1-(1-oxopropoxy)propoxy](4-phenylbutyl)phosphinyl]acetyl]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

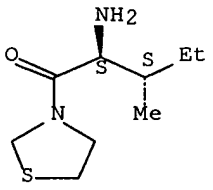


RN 251572-86-8 HCAPLUS
CN Thiazolidine, 3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]-, (2E)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 136259-20-6
CMF C9 H18 N2 O S
CDES 1:S2:R*,R*

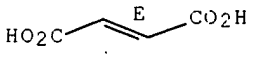
Absolute stereochemistry.



CM 2

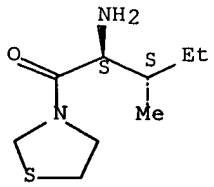
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



L16 ANSWER 11 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:894621 HCAPLUS
DN 135:40770
TI DP IV-inhibitors: potential antidiabetic drugs
AU Schlenzig, D.; Kruber, S.; White, H. A.; Pederson, R. A.; Demuth, H. -U.
CS Probiodrug Gesellschaft fur Arzneimittelforschung mbH, Halle, 06120, Germany
SO Peptides for the New Millennium, Proceedings of the American Peptide Symposium, 16th, Minneapolis, MN, United States, June 26-July 1, 1999 (2000), Meeting Date 1999, 224-226. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Publisher: Kluwer Academic Publishers, Dordrecht, Neth.
CODEN: 69ATHX
DT Conference
LA English
AB The proline specific exopeptidase dipeptidylpeptidase IV (DP IV) is able to release dipeptides from peptides if proline, alanine, or hydroxyproline are present in the penultimate position of the N-terminus. Hence, the enzyme plays an important role in the regulation of the biol. activity of several peptide hormones. The incretins glucagon-like peptide-1 [GLP-1(7-36)amide] and glucose-dependent insulinotropic peptide (GIP) have proven to be natural substrates of DP IV. The goal of the study was to show that isoleucyl-thiazolide, a highly specific competitive inhibitor of DP IV, might be a useful compd. to serve as a lead structure for creating a new class of orally available antidiabetic drugs for non-insulin dependent **diabetes** mellitus (NIDDM). Therefore, the resorption of orally administered Ile-thiazolide in rats and the effect of orally administered Ile-thiazolide on insulin secretion after an oral glucose intake in obese and lean Zucker rats, were investigated. Results indicated that Ile-thiazolide might be a lead for the development of a new class of oral antidiabetics for the management of NIDDM.
IT **136259-20-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dipeptidylpeptidase IV-inhibitors: potential antidiabetic drugs)
RN 136259-20-6 HCAPLUS
CN Thiazolidine, 3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **54249-88-6**, dipeptidylpeptidase IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(dipeptidylpeptidase IV-**inhibitors**: potential antidiabetic drugs)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 12 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:841992 HCAPLUS
DN 134:13324
TI Boroproline compounds for inhibiting cell proliferation and angiogenesis and treating **tumors**
IN Wallner, Barbara P.; Miller, Glenn
PA Point Therapeutics, Inc., USA
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

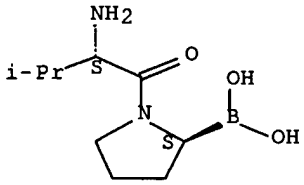
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000071135	A1	20001130	WO 2000-US14505	20000525
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1187619	A1	20020320	EP 2000-937801	20000525
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	US 1999-135861P	P	19990525		
	WO 2000-US14505	W	20000525		

AB A method for treating subjects with abnormal cell proliferation is provided. The method involves administering to subjects in need of such treatment an effective amt. of an agent PR [P is a targeting group which binds to the reactive site of fibroblast activation protein .alpha. (FAP-.alpha.) or other post proline cleaving enzyme and can be a peptide or peptidomimetic; R is a reactive group capable of reacting with a functional group in FAP-.alpha. or other post proline cleaving enzyme, preferably in the reactive site] (I) to inhibit cell proliferation, e.g. that assocd. with **tumor** growth and metastasis. A method for inhibiting angiogenesis in an abnormal proliferative cell mass by the administration of I is also provided. The preferred compds. are boroproline derivs.
IT **54249-88-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(boroproline compds. for **inhibiting** cell proliferation and angiogenesis and treating **tumors**)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

IT **174276-10-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(boroproline compds. for inhibiting cell proliferation and angiogenesis and treating **tumors**)
RN 174276-10-9 HCAPLUS
CN Boronic acid, [(2S)-1-[(2S)-2-amino-3-methyl-1-oxobutyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



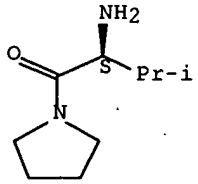
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 13 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:622123 HCAPLUS
DN 133:359069
TI Improved glucose tolerance and insulin secretion by inhibition of dipeptidyl peptidase IV in mice
AU Ahren, B.; Holst, J. J.; Martensson, H.; Balkan, B.
CS Malmo University Hospital, Department of Medicine, Lund University, Malmo, S-205 02, Swed.
SO European Journal of Pharmacology (2000), 404(1/2), 239-245
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
AB We explored whether inhibition of the enzyme dipeptidyl peptidase IV (DPP IV) increases endogenous levels of glucagon-like peptide-1 (GLP-1) and improves glucose tolerance and insulin secretion in mice. Glucose (150 mg) was administered through a gastric gavage with or without the inhibitor of dipeptidyl peptidase IV, valine-pyrrolidide (100 .mu.mol/kg), in high-fat fed glucose intolerant or control C57BL/6J mice. The increase in plasma GLP-1 after gastric glucose was potentiated by dipeptidyl peptidase IV inhibition ($P<0.05$). Valine-pyrrolidide also potentiated the plasma insulin response to gastric glucose and improved the glucose tolerance in both groups of mice ($P<0.001$). In contrast, valine-pyrrolidide did not affect glucose-stimulated insulin secretion from isolated islets. This suggests that valine-pyrrolidide improves insulin secretion and glucose tolerance through indirect action, probably through augmentation of levels of GLP-1 and other incretin hormones. Therefore, inhibition of dipeptidyl peptidase IV activity is feasible to exploit as a treatment for glucose intolerance and type 2 **diabetes**.

IT **54164-07-7**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dipeptidyl peptidase IV inhibition: improved glucose tolerance and

insulin secretion)
RN 54164-07-7 HCAPLUS
CN Pyrrolidine, 1-[(2S)-2-amino-3-methyl-1-oxobutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



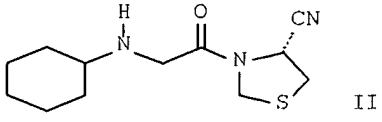
IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(dipeptidyl peptidase IV **inhibition**: improved glucose tolerance and insulin secretion)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 14 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:606862 HCAPLUS
DN 133:193135
TI Preparation of 3-[(alkylamino)acetyl]-4-cyanothiazolidines as dipeptidyl peptidase IV inhibitors
IN Villhauer, Edwin Bernard
PA Novartis A.-G., Switz.
SO U.S., 11 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6110949	A	20000829	US 1999-339503	19990624

OS MARPAT 133:193135
GI



II

AB RNHCH2COR5 [I; R = (cyclo)alkyl, CH2CH2NHR1, CH2CH2R2, CH2CH2CH(R3)2, (CH2)3R4; R1 = (un)substituted pyridinyl or.-pyrimidinyl; R2,R3 = (un)substituted Ph; R4 = 2-oxopyrrolidinyl or alkoxy; R5 = (R)-4-cyano-3-thiazolidinyl] were prepd. Thus, (R)-thiazolidine-4-carboxamide was N-acylated by Me3CO2CNRCH2CO2H (R = cyclohexyl)(prepn.

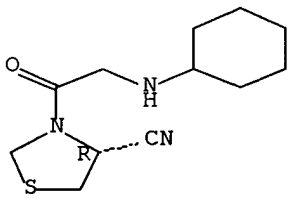
each given) and the product dehydrated to give, after deprotection, title compd. II. Data for biol. activity of I were given.

IT **54249-88-6**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(mediated disorders; treatment; prepn. of 3-[(alkylamino)acetyl]-4-cyanothiazolidines as dipeptidyl peptidase IV **inhibitors**)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

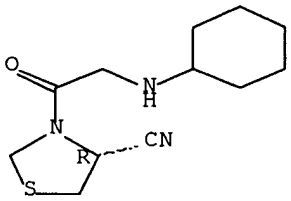
IT **289480-99-5P 289481-00-1P 289481-01-2P**
289481-02-3P 289481-03-4P 289481-04-5P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-[(alkylamino)acetyl]-4-cyanothiazolidines as dipeptidyl peptidase IV inhibitors)
RN 289480-99-5 HCAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[(cyclohexylamino)acetyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 289481-00-1 HCAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[(cyclohexylamino)acetyl]-, monohydrochloride, (4R)- (9CI) (CA INDEX NAME)

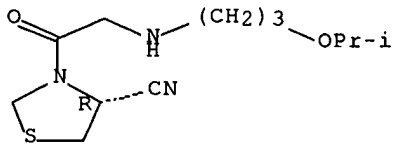
Absolute stereochemistry.



● HCl

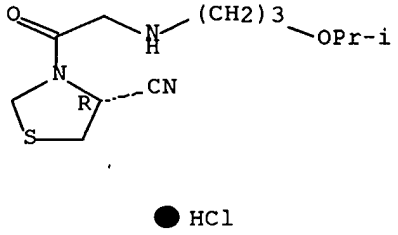
RN 289481-01-2 HCAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[[[3-(1-methylethoxy)propyl]amino]acetyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 289481-02-3 HCAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[[[3-(1-methylethoxy)propyl]amino]acetyl]-, monohydrochloride, (4R)- (9CI) (CA INDEX NAME)

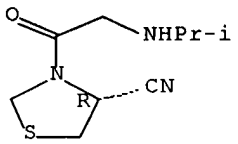
Absolute stereochemistry.



● HCl

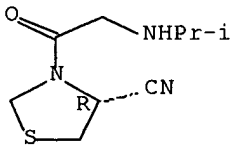
RN 289481-03-4 HCAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[[(1-methylethyl)amino]acetyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 289481-04-5 HCAPLUS
CN 4-Thiazolidinecarbonitrile, 3-[[(1-methylethyl)amino]acetyl]-, monohydrochloride, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

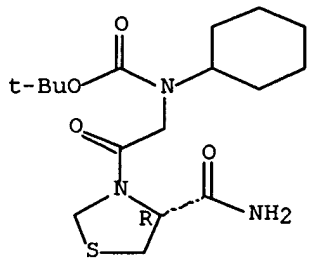
IT **289481-05-6P 289481-06-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. of 3-[(alkylamino)acetyl]-4-cyanothiazolidines as dipeptidyl peptidase IV inhibitors)

RN 289481-05-6 HCAPLUS

CN Carbamic acid, [2-[(4R)-4-(aminocarbonyl)-3-thiazolidinyl]-2-oxoethyl]cyclohexyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

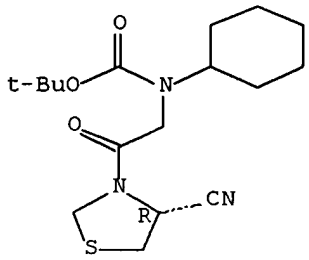
Absolute stereochemistry.



RN 289481-06-7 HCAPLUS

CN Carbamic acid, [2-[(4R)-4-cyano-3-thiazolidinyl]-2-oxoethyl]cyclohexyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 15 OF 30 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:401789 HCAPLUS

DN 133:43431

TI Preparation of N-glycyl-2-cyanopyrrolidines as DPP IV inhibitors

IN Villhauer, Edwin Bernard

PA Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.

SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000034241	A1	20000615	WO 1999-EP9708	19991209

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,

CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6166063	A	20001226	US 1999-458224	19991209	
BR 9915985	A	20010904	BR 1999-15985	19991209	
EP 1137635	A1	20011004	EP 1999-959396	19991209	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO					
NO 2001002853	A	20010807	NO 2001-2853	20010608	
PRAI US 1998-209068	A	19981210			
WO 1999-EP9708	W	19991209			

OS MARPAT 133:43431

AB R(CH2)nNHCH2COZCN [Z = (S)-pyrrolidine-1,2-diyl](I; R = substituted adamantyl; n = 0-3) were prepd. Thus, L-prolineamide was treated successively with ClCH2COCl and (CF3CO)2O and the product aminated by 1-aminoadamantan-3-ol (prepn. given) to give I (R = 3-hydroxy-1-adamantylamino, n = 0)(II). Data for biol. activity of II were given.

IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mediated disorders; treatment; prepn. of N-glycyl-2-cyanopyrrolidines as DPP IV **inhibitors**)

RN 54249-88-6 HCAPLUS

CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

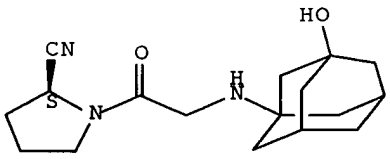
*** STRUCTURE DIAGRAM IS NOT AVAILABLE

IT **274901-16-5P 274901-17-6P 274901-18-7P**
274901-19-8P 274901-20-1P 274901-21-2P
274901-22-3P 274901-24-5P 274901-25-6P
274901-26-7P 274901-27-8P 274901-28-9P
274901-29-0P 274901-30-3P 274901-31-4P
274901-32-5P 274901-33-6P 274901-34-7P
274901-35-8P 274901-36-9P 275354-26-2P
275354-27-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-glycyl-2-cyanopyrrolidines as DPP IV inhibitors)

RN 274901-16-5 HCAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[(3-hydroxytricyclo[3.3.1.13,7]dec-1-yl)amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

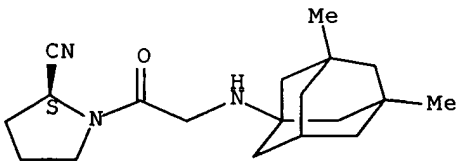
Absolute stereochemistry.



RN 274901-17-6 HCAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[(3,5-dimethyltricyclo[3.3.1.13,7]dec-1-yl)amino]acetyl]-, monohydrochloride, (2S)- (9CI) (CA INDEX NAME)

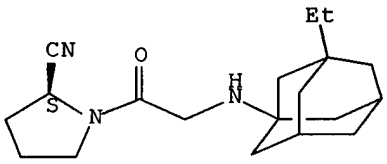
Absolute stereochemistry.



● HCl

RN 274901-18-7 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[(3-ethyltricyclo[3.3.1.13,7]dec-1-yl)amino]acetyl]-, monohydrochloride, (2S)- (9CI) (CA INDEX NAME)

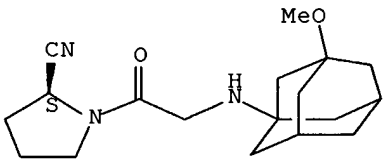
Absolute stereochemistry.



● HCl

RN 274901-19-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[(3-methoxytricyclo[3.3.1.13,7]dec-1-yl)amino]acetyl]-, monohydrochloride, (2S)- (9CI) (CA INDEX NAME)

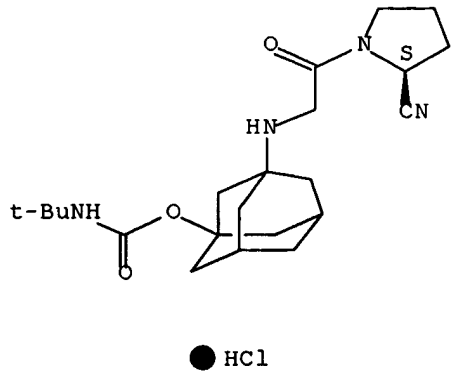
Absolute stereochemistry.



● HCl

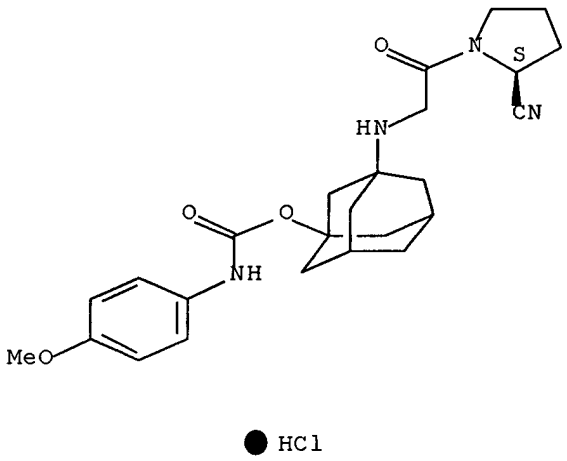
RN 274901-20-1 HCAPLUS
CN Carbamic acid, (1,1-dimethylethyl)-, 3-[[2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



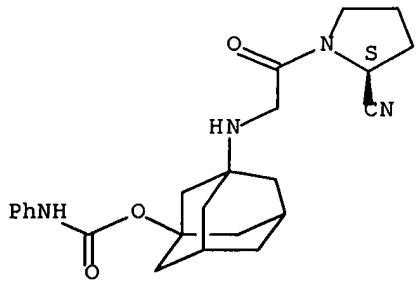
RN 274901-21-2 HCAPLUS
CN Carbamic acid, (4-methoxyphenyl)-, 3-[[2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 274901-22-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[3-[[(phenylamino)carbonyl]oxy]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, monohydrochloride, (2S)- (9CI) (CA INDEX NAME)

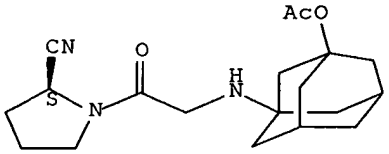
Absolute stereochemistry.



● HCl

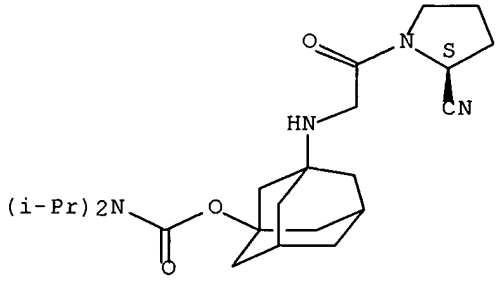
RN 274901-24-5 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[3-(acetyloxy)tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 274901-25-6 HCAPLUS
CN Carbamic acid, bis(1-methylethyl)-, 3-[[2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

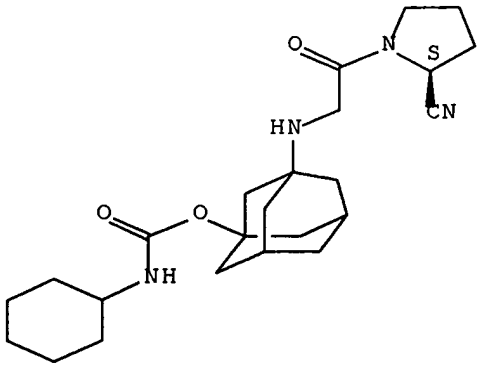
Absolute stereochemistry.



● HCl

RN 274901-26-7 HCAPLUS
CN Carbamic acid, cyclohexyl-, 3-[[2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

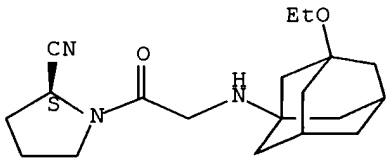
Absolute stereochemistry.



● HCl

RN 274901-27-8 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[(3-ethoxytricyclo[3.3.1.13,7]dec-1-yl)amino]acetyl]-, monohydrochloride, (2S)- (9CI) (CA INDEX NAME)

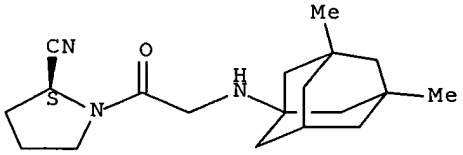
Absolute stereochemistry.



● HCl

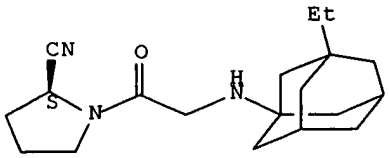
RN 274901-28-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[(3,5-dimethyltricyclo[3.3.1.13,7]dec-1-yl)amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



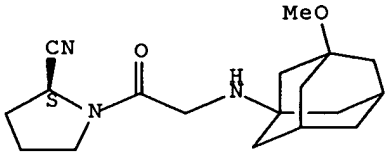
RN 274901-29-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[(3-ethyltricyclo[3.3.1.13,7]dec-1-yl)amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



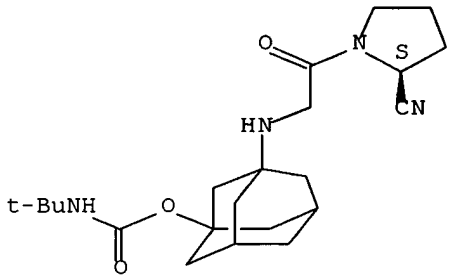
RN 274901-30-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[(3-methoxytricyclo[3.3.1.13,7]dec-1-yl)amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



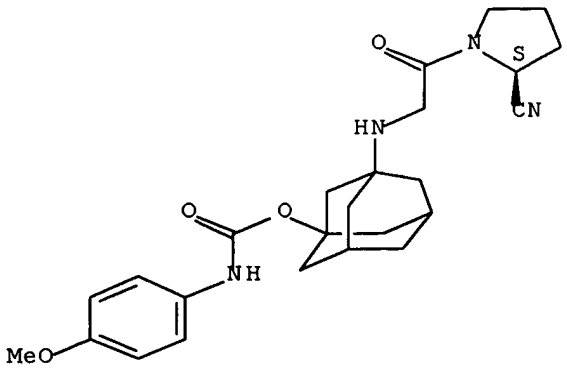
RN 274901-31-4 HCAPLUS
CN Carbamic acid, (1,1-dimethylethyl)-, 3-[[2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



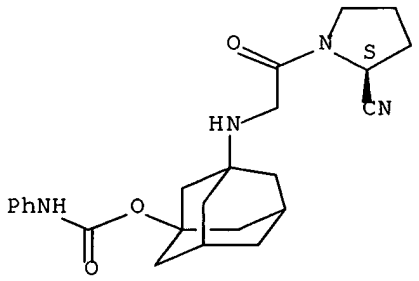
RN 274901-32-5 HCAPLUS
CN Carbamic acid, (4-methoxyphenyl)-, 3-[[2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



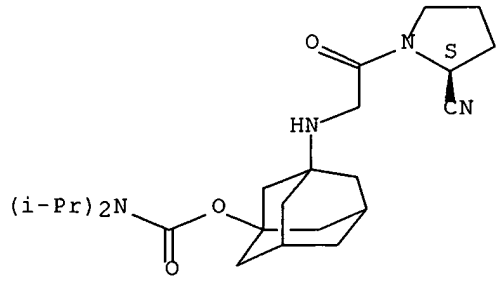
RN 274901-33-6 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[3-[[(phenylamino)carbonyl]oxy]tricyclo[3.3.1.13,7]dec-1-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



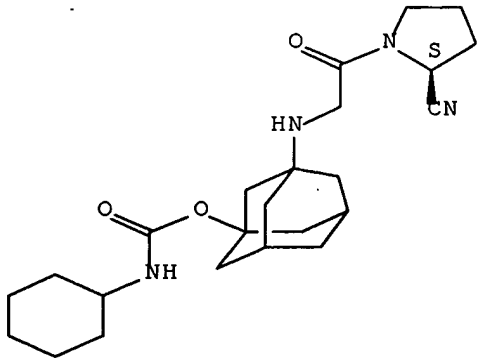
RN 274901-34-7 HCAPLUS
CN Carbamic acid, bis(1-methylethyl)-, 3-[[2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



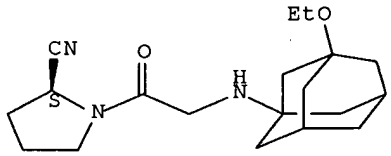
RN 274901-35-8 HCAPLUS
CN Carbamic acid, cyclohexyl-, 3-[[2-[(2S)-2-cyano-1-pyrrolidinyl]-2-oxoethyl]amino]tricyclo[3.3.1.13,7]dec-1-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



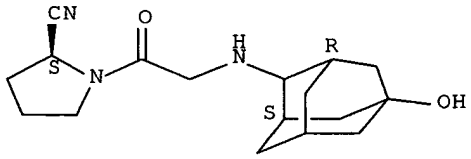
RN 274901-36-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[(3-ethoxytricyclo[3.3.1.13,7]dec-1-yl)amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



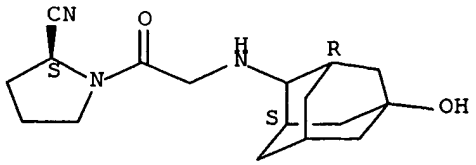
RN 275354-26-2 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[(5-hydroxytricyclo[3.3.1.13,7]dec-2-yl)amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



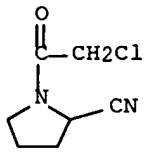
RN 275354-27-3 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[(5-hydroxytricyclo[3.3.1.13,7]dec-2-yl)amino]acetyl]-, monohydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



HCl

IT **274901-37-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of N-glycyl-2-cyanopyrrolidines as DPP IV inhibitors)
RN 274901-37-0 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-(chloroacetyl)- (9CI) (CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 16 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:819401 HCAPLUS
DN 132:36037
TI Synthesis and use of prodrugs of dipeptidyl peptidase IV inhibitors
IN Demuth, Hans-Ulrich; Hoffmann, Torsten; Schlenzig, Dagmar; Manhart, Susanne
PA Probiodrug Gesellschaft fur Arzneimittelforschung m.b.H., Germany
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9967278	A1	19991229	WO 1999-EP4382	19990624
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 19828113	A1	20000105	DE 1998-19828113	19980624
	AU 9949007	A1	20000110	AU 1999-49007	19990624
	BR 9911468	A	20010320	BR 1999-11468	19990624
	EP 1087991	A1	20010404	EP 1999-932721	19990624
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NO 2000006484	A	20001219	NO 2000-6484	20001219
PRAI	DE 1998-19828113	A	19980624		
	WO 1999-EP4382	W	19990624		

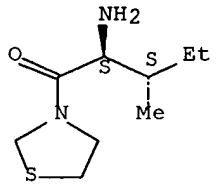
OS MARPAT 132:36037
AB The invention relates to prodrug compds. of inhibitors of dipeptidyl peptidase IV (DP IV). Said prodrug compds. comprise general formulas (A-B-C), whereby A represents an amino acid, B represents the chem. bond

between A and C or an amino acid, and C represents a stabile inhibitor of DP IV. Such prodrug compds. are used for treating altered glucose tolerance, glucosuria, hyperlipidemia, metabolic acidosis, **diabetes** mellitus, **diabetic** neuropathy, nephropathy, and secondary diseases in mammals caused by **diabetes** mellitus. Thus, Boc-Pro-Ile-OH was coupled with thiazolidine, N-deprotected, reacted with Boc-Gy-OH, and then N-deprotected to give H-Gly-Pro-Ile-R (R = thiazolidine) (I). In in vivo tests using Wister rats, H-Ile-R, I, and H-Pro-Ile-R gave blood glucose levels of 74.4, 57.1, and 56.1% (compared to control = 100%) at doses of 2.5.mu.M/300 g wt.

IT **136259-20-6 252348-25-7 252348-26-8 252348-27-9**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biol. activity of as prodrugs of dipeptidyl peptidase IV inhibitors)

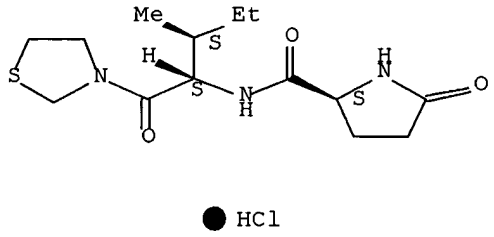
RN 136259-20-6 HCAPLUS
CN Thiazolidine, 3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



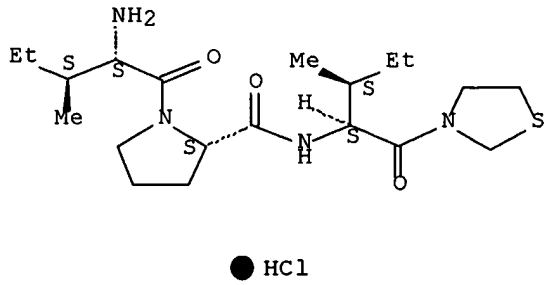
RN 252348-25-7 HCAPLUS
CN 2-Pyrrolidinecarboxamide, N-[(1S,2S)-2-methyl-1-(3-thiazolidinylcarbonyl)butyl]-5-oxo-, monohydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 252348-26-8 HCAPLUS
CN L-Prolinamide, L-isoleucyl-N-[(1S,2S)-2-methyl-1-(3-thiazolidinylcarbonyl)butyl]-, monohydrochloride (9CI) (CA INDEX NAME)

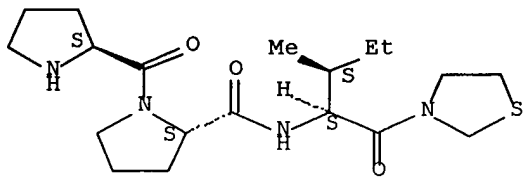
Absolute stereochemistry.



● HCl

RN 252348-27-9 HCAPLUS
CN L-Prolinamide, L-prolyl-N-[(1S,2S)-2-methyl-1-(3-thiazolidinylcarbonyl)butyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

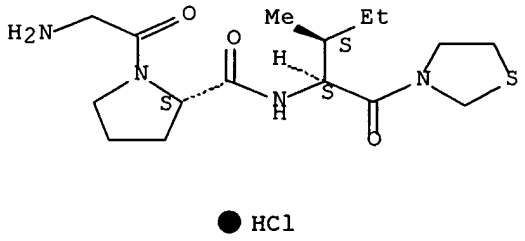


● HCl

IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**inhibition** of by prodrugs for treatment of disease)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
IT **252348-24-6P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and biol. activity of in the synthesis and use of prodrugs of dipeptidyl peptidase IV inhibitors)
RN 252348-24-6 HCAPLUS
CN L-Prolinamide, glycyl-N-[(1S,2S)-2-methyl-1-(3-thiazolidinylcarbonyl)butyl]-, monohydrochloride (9CI) (CA INDEX NAME)

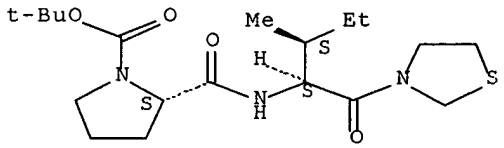
Absolute stereochemistry.



● HCl

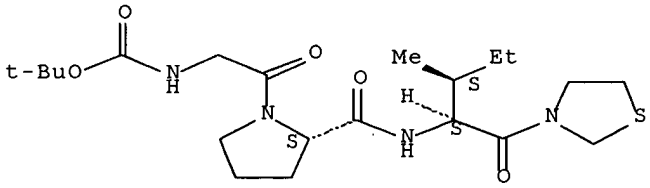
IT **252348-21-3P 252348-22-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of in the synthesis and use of prodrugs of dipeptidyl peptidase IV inhibitors)
RN 252348-21-3 HCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2-[[[(1S,2S)-2-methyl-1-(3-thiazolidinylcarbonyl)butyl]amino]carbonyl]-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



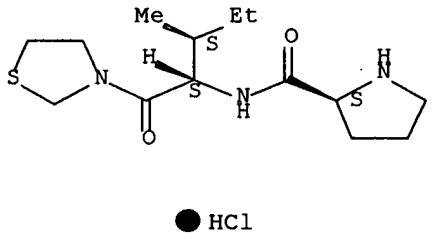
RN 252348-22-4 HCAPLUS
CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]glycyl-N-[(1S,2S)-2-methyl-1-(3-thiazolidinylcarbonyl)butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **252348-23-5P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn., reaction, and biol. activity of in the synthesis and use of prodrugs of dipeptidyl peptidase IV inhibitors)
RN 252348-23-5 HCAPLUS
CN 2-Pyrrolidinecarboxamide, N-[(1S,2S)-2-methyl-1-(3-thiazolidinylcarbonyl)butyl]-, monohydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



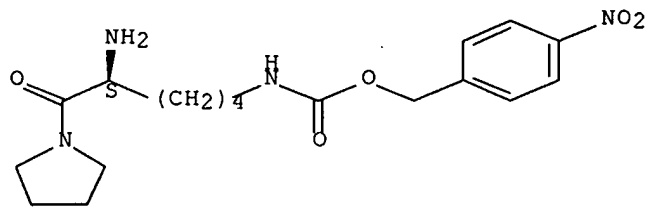
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 17 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:811521 HCAPLUS
DN 132:45004
TI Dipeptidyl dipeptidase IV (DPIV) inhibitor-based methods and pharmaceutical preparations for the therapy of skin diseases with follicular and epidermal hyperkeratosis and increased keratinocyte proliferation
IN Ansorge, Siegfried; Born, Ilona; Buhling, Frank; Faust, Jurgen; Gollnick, Harald; Lendeckel, Uwe; Neubert, Klaus; Reinhold, Dirk; Vetter, Robert
PA Otto-Von-Guericke-Universitat Magdeburg, Germany; Martin-Luther-Universitat Halle-Wittenberg
SO Ger. Offen., 6 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 19826972	A1	19991223	DE 1998-19826972	19980618

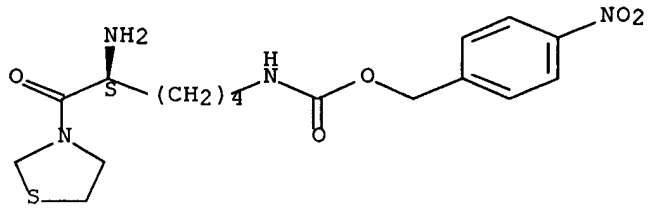
AB The invention provides a method in which, through inhibition of human keratinocyte-expressed DPIV (EC 3.4.14.5; CD26) by corresponding specific inhibitors, the activation and DNA synthesis and thus the proliferation of these cells is suppressed. The methodol. and prepns. of the invention can be used for supportive therapy for e.g. inflammatory and noninflammatory epidermal hyperproliferative conditions (e.g. congenital ichthyosis and psoriasis), benign and malignant localized epidermal clonal expansions (e.g. warts, condylomas, actinic keratoses), benign and malignant hyperproliferative conditions (e.g. acne). as well as benign and malignant epithelial adnexal **tumors** and primary and reactive nail cell hyperproliferation.
IT **136259-18-2 136259-19-3 252860-56-3**
252860-57-4
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dipeptidyl peptidase IV (DPIV) inhibitor-based methods and pharmaceutical prepns. for therapy of skin diseases with follicular and epidermal hyperkeratosis and increased keratinocyte proliferation)
RN 136259-18-2 HCAPLUS
CN Carbamic acid, [(5S)-5-amino-6-oxo-6-(1-pyrrolidinyl)hexyl]-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



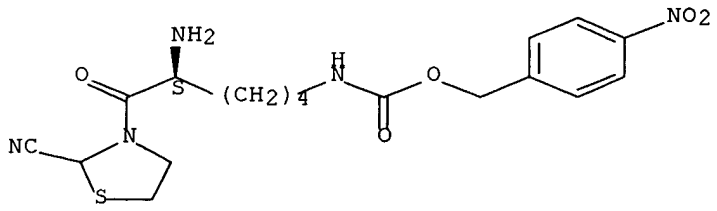
RN 136259-19-3 HCAPLUS
CN Carbamic acid, [(5S)-5-amino-6-oxo-6-(3-thiazolidinyl)hexyl]-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



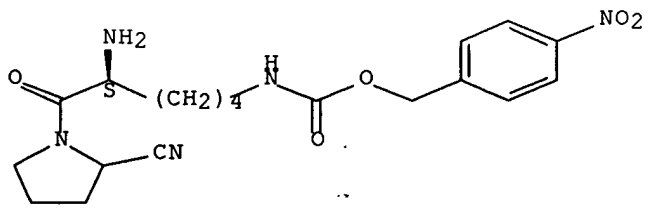
RN 252860-56-3 HCAPLUS
CN Carbamic acid, [(5S)-5-amino-6-(2-cyano-3-thiazolidinyl)-6-oxohexyl]-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 252860-57-4 HCAPLUS
CN Carbamic acid, [(5S)-5-amino-6-(2-cyano-1-pyrrolidinyl)-6-oxohexyl]-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **54249-88-6**, e.c. 3.4.14.5
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(dipeptidyl peptidase IV (DPIV) **inhibitor**-based methods and pharmaceutical prepns. for therapy of skin diseases with follicular and epidermal hyperkeratosis and increased keratinocyte proliferation)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 18 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:764028 HCAPLUS
DN 132:15632
TI New dipeptidyl peptidase IV effectors
IN Demuth, Hans-Ulrich; Glund, Konrad; Schlenzig, Dagmar; Kruber, Susanne
PA Probiodrug Gesellschaft Fur Arzneimittelforschung m.b.H., Germany
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9961431	A1	19991202	WO 1999-EP3712	19990528
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 19823831	A1	19991202	DE 1998-19823831	19980528
	AU 9943709	A1	19991213	AU 1999-43709	19990528
	BR 9910758	A	20010213	BR 1999-10758	19990528
	EP 1082314	A1	20010314	EP 1999-926464	19990528
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NO 2000005994	A	20010125	NO 2000-5994	20001127
PRAI	DE 1998-19823831	A	19980528		
	WO 1999-EP3712	W	19990528		

AB Dipeptides and their analogs comprising an amino acid and a thiazolidine or pyrrolidine group, and their salts, are useful in the oral or parenteral treatment of impaired glucose tolerance, glucosuria, hyperlipidemia, metabolic acidosis, **diabetes** mellitus, **diabetic** neuropathy and nephropathy, as well as diseases secondary to **diabetes** mellitus in mammals. These dipeptides inhibit dipeptidyl peptidase IV, a blood enzyme which cleaves N-terminal dipeptides from glucose-dependent insulinotropic polypeptides such as gastric inhibitory polypeptide(1-42) and glucagon-like peptide amide-1(7-36) which stimulate glucose-induced insulin secretion by the pancreas, as well as similar enzymes. Thus, oral administration of 20 .mu.M L-allo-isoleucine thiazolidide to **diabetic** rats during a glucose tolerance test decreased the blood glucose concn. to 73% of control values within 60 min. Tablets were prepd. by granulating a mixt.

of L-allo-isoleucine thiazolidide-HCl 10.0, glucose 4.35, lactose 4.35, starch 4.50, and cellulose 4.50 kg with a soln. of PVP 2.0 and polysorbate 0.1 in H2O 5.0 kg, adding 0.2 kg Mg stearate, and pressing into 300-mg tablets.

IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**inhibitors**; new dipeptidyl peptidase IV effectors)

RN 54249-88-6 HCAPLUS

CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

IT **54164-07-7 56414-88-1 65627-83-0**
136259-20-6 136259-21-7 136259-22-8
177746-67-7 177746-72-4 177931-21-4
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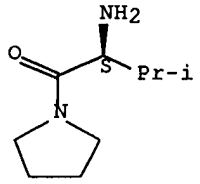
251573-62-3 251573-63-4 251573-64-5
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new dipeptidyl peptidase IV effectors)

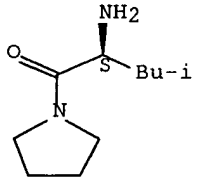
RN 54164-07-7 HCAPLUS
CN Pyrrolidine, 1-[(2S)-2-amino-3-methyl-1-oxobutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



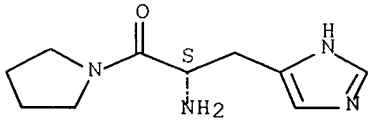
RN 56414-88-1 HCAPLUS
CN Pyrrolidine, 1-[(2S)-2-amino-4-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



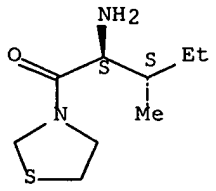
RN 65627-83-0 HCAPLUS
CN Pyrrolidine, 1-[(2S)-2-amino-3-(1H-imidazol-4-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



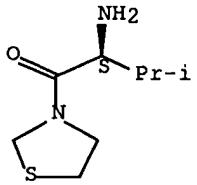
RN 136259-20-6 HCAPLUS
CN Thiazolidine, 3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



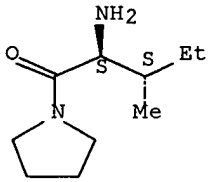
RN 136259-21-7 HCAPLUS
CN Thiazolidine, 3-[(2S)-2-amino-3-methyl-1-oxobutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



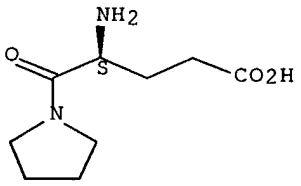
RN 136259-22-8 HCAPLUS
CN Pyrrolidine, 1-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



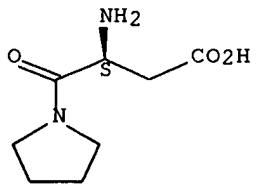
RN 177746-67-7 HCAPLUS
CN 1-Pyrrolidinepentanoic acid, .gamma.-amino-.delta.-oxo-, (.gamma.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



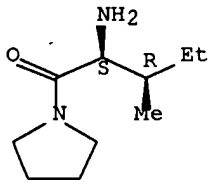
RN 177746-72-4 HCAPLUS
CN 1-Pyrrolidinebutanoic acid, .beta.-amino-.gamma.-oxo-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



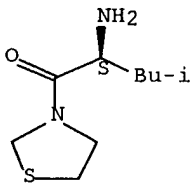
RN 177931-21-4 HCAPLUS
CN Pyrrolidine, 1-[(2S,3R)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



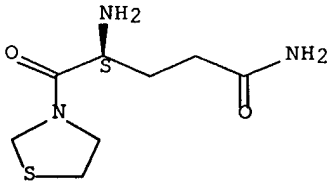
RN 251571-73-0 HCAPLUS
CN Thiazolidine, 3-[(2S)-2-amino-4-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 251571-74-1 HCAPLUS
CN 3-Thiazolidinepentanamide, .gamma.-amino-.delta.-oxo-, (.gamma.S)- (9CI) (CA INDEX NAME)

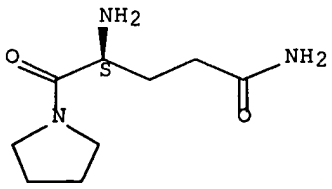
Absolute stereochemistry.



RN 251571-75-2 HCAPLUS
CN 1-Pyrrolidinepentanamide, .gamma.-amino-.delta.-oxo-, (.gamma.S)- (9CI)

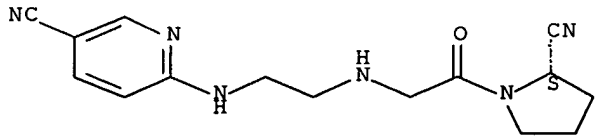
(CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:699517 HCAPLUS
DN 131:318094
TI Inhibition of dipeptidyl peptidase IV with NVP-DPP728 increases plasma GLP-1 (7-36 amide) concentrations and improves oral glucose tolerance in obese Zucker rats
AU Balkan, B.; Kwasnik, L.; Miserendino, R.; Holst, J. J.; Li, X.
CS Novartis Institute Biomedical Research, Summit, NJ, 07901, USA
SO Diabetologia (1999), 42(11), 1324-1331
CODEN: DBTGAJ; ISSN: 0012-186X
PB Springer-Verlag
DT Journal
LA English
AB The potent incretin hormone glucagon-like peptide 1 (GLP-1) plays a pivotal role in prandial insulin secretion. In the circulation GLP-1 (7-36) amide is, however, rapidly (t1/2: 1-2 min) inactivated by the protease dipeptidyl peptidase IV (DPP-IV). We therefore investigated whether DPP-IV inhibition is a feasible approach to improve glucose homeostasis in insulin resistant, glucose intolerant fatty Zucker rats, a model of mild Type II (non-insulin-dependent) **diabetes** mellitus. An oral glucose tolerance test was done in lean and obese male Zucker rats while plasma DPP-IV was inhibited by the specific and selective inhibitor NVP-DPP728 given orally. Inhibition of DPP-IV resulted in a significantly amplified early phase of the insulin response to an oral glucose load in obese falfa rats and restoration of glucose excursions to normal. In contrast, DPP-IV inhibition produced only minor effects in lean FA/ rats. Inactivation of GLP-1 (7-36) amide was completely prevented by DPP-IV inhibition suggesting that the effects of this compd. on oral glucose tolerance are mediated by increased circulating concns. of GLP-1 (7-36) amide. Reduced gastric emptying, as monitored by paracetamol appearance in the circulation after an oral bolus, did not appear to have contributed to the reduced glucose excursion. It is concluded that NVP-DPP728 inhibits DPP-IV and improves insulin secretion and glucose tolerance, probably through augmentation of the effects of endogenous GLP-1. The improvement obsd. in prandial glucose homeostasis during DPP-IV inhibition suggests that inhibition of this enzyme is a promising treatment for Type II **diabetes**.
IT **247016-69-9**, NVP-DPP 728
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of dipeptidyl peptidase IV with NVP-DPP728 increases plasma GLP-1 concns. and improves oral glucose tolerance in obese Zucker rats)
RN 247016-69-9 HCAPLUS
CN 2-Pyrrolidinecarbonitrile, 1-[[[2-[(5-cyano-2-pyridinyl)amino]ethyl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**inhibition** of dipeptidyl peptidase IV with NVP-DPP728 increases plasma GLP-1 concns. and improves oral glucose tolerance in obese Zucker rats)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 20 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:495164 HCAPLUS
DN 131:139502
TI Method of regulating glucose metabolism, and reagents related thereto
IN Bachovchin, William W.; Plaut, Andrew G.; Drucker, Daniel J.
PA Trustees of Tufts University, USA
SO PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9938501	A2	19990805	WO 1999-US2294	19990202
	WO 9938501	A3	20000113		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9924935	A1	19990816	AU 1999-24935	19990202
	EP 1052994	A2	20001122	EP 1999-904558	19990202
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002501889	T2	20020122	JP 2000-529234	19990202
PRAI	US 1998-73409P	P	19980202		
	WO 1999-US2294	W	19990202		

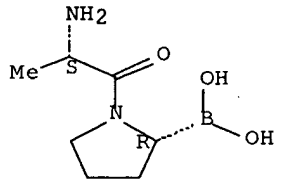
OS MARPAT 131:139502
AB The present invention provides methods and compns. for modification and regulation of glucose and lipid metab., generally to reduce insulin resistance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia,

hyperlipoproteinemia (such as chylomicrons, VLDL and LDL), and to regulate body fat and more generally lipid stores, and, more generally, for the improvement of metab. disorders, esp. those assocd. with **diabetes**, obesity and/or atherosclerosis.

IT **54249-88-6**, Dipeptidylpeptidase IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; method of regulating glucose metab., and reagents related thereto)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

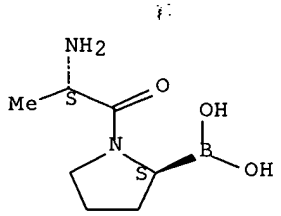
*** STRUCTURE DIAGRAM IS NOT AVAILABLE
IT **139649-82-4P 139649-83-5P**
RL: PNU (Preparation, unclassified); PREP (Preparation)
(method of regulating glucose metab., and reagents related thereto)
RN 139649-82-4 HCAPLUS
CN Boronic acid, [(2R)-1-[(2S)-2-amino-1-oxopropyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



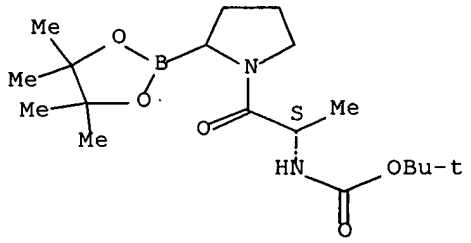
RN 139649-83-5 HCAPLUS
CN Boronic acid, [(2S)-1-[(2S)-2-amino-1-oxopropyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



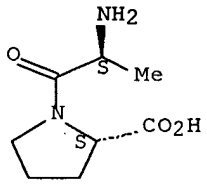
IT **235085-95-7P**
RL: PNU (Preparation, unclassified); RCT (Reactant); PREP (Preparation)
(method of regulating glucose metab., and reagents related thereto)
RN 235085-95-7 HCAPLUS
CN Carbamic acid, [(1S)-1-methyl-2-oxo-2-[2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-pyrrolidinyl]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **13485-59-1**, Alanylproline
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peptidomimetics of; method of regulating glucose metab., and reagents related thereto)
RN 13485-59-1 HCAPLUS
CN L-Proline, L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 21 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:233987 HCAPLUS
DN 130:264434
TI Stimulation of hematopoietic cells in vitro using inhibitors of dipeptidyl peptidase IV in the absence of cytokines
IN Bachovchin, William; Wallner, Barbara
PA Point Therapeutics, Inc., USA
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9916864	A1	19990408	WO 1998-US20343	19980929
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9895887	A1	19990423	AU 1998-95887	19980929
	EP 1019494	A1	20000719	EP 1998-949595	19980929
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	BR 9813233	A	20000822	BR 1998-13233	19980929
	US 6258597	B1	20010710	US 1998-162934	19980929

	JP 2001518290	T2	20011016	JP 2000-513935	19980929
	NO 2000001583	A	20000529	NO 2000-1583	20000327
	US 2001018210	A1	20010830	US 2001-812528	20010320
PRAI	US 1997-60306P	P	19970929		
	US 1998-162934	A1	19980929		
	WO 1998-US20343	W	19980929		

AB The present invention provides methods and compns. for stimulating the growth and differentiation of hematopoietic cells in vitro. Advantageously, the methods of the invention do not require the addn. of exogenously added cytokines to support the stimulation of hematopoietic cells in vitro. The methods involve contacting the hematopoietic cells with an inhibitor of dipeptidyl peptidase (DPIV) in the absence of exogenously provided cytokines. Accordingly, the methods and compns. of the invention are useful for increasing the no. of hematopoietic cells in vitro and/or causing the differentiation of early progenitor cells. The stimulated hematopoietic cells of the invention are useful for the treatment of disorders that are characterized by a reduced no. of hematopoietic cells or their precursors in vivo. Such conditions occur frequently in patients who are immunosuppressed, for example, as a consequence of chemotherapy and/or radiation therapy for cancer.

IT **54249-88-6,** Dipeptidyl peptidase IV
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**inhibitor**; stimulation of hematopoietic cells in vitro using **inhibitors** of dipeptidyl peptidase IV in the absence of cytokines)

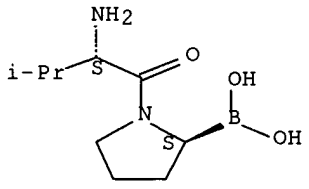
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

IT **174276-10-9 202203-06-3 202203-06-3D,**
conjugate
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(stimulation of hematopoietic cells in vitro using inhibitors of dipeptidyl peptidase IV in the absence of cytokines)

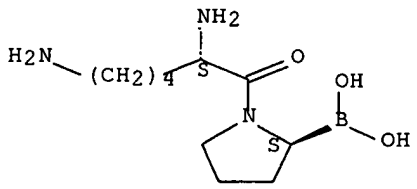
RN 174276-10-9 HCAPLUS
CN Boronic acid, [(2S)-1-[(2S)-2-amino-3-methyl-1-oxobutyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



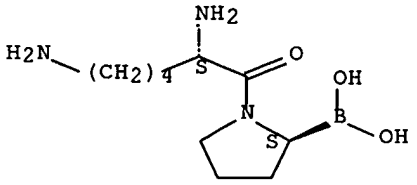
RN 202203-06-3 HCAPLUS
CN Boronic acid, [(2S)-1-[(2S)-2,6-diamino-1-oxohexyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 202203-06-3 HCAPLUS
CN Boronic acid, [(2S)-1-[(2S)-2,6-diamino-1-oxohexyl]-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



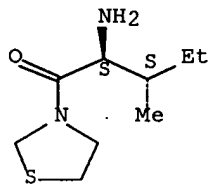
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 22 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:192883 HCAPLUS
DN 131:508
TI Improved glucose tolerance in rats treated with the dipeptidyl peptidase IV (CD26) inhibitor Ile-thiazolidide
AU Pauly, Robert P.; Demuth, Hans-Ulrich; Rosche, Fred; Schmidt, Jorn; White, Heather A.; Lynn, Francis; McIntosh, Christopher H. S.; Pederson, Raymond A.
CS Department of Physiology, University of British Columbia, Vancouver, BC, BC V6T 1Z3, Can.
SO Metab., Clin. Exp. (1999), 48(3), 385-389
CODEN: METAAJ; ISSN: 0026-0495
PB W. B. Saunders Co.
DT Journal
LA English
AB The incretins glucose-dependent insulinotropic polypeptide (GIP1-42) and truncated forms of glucagon-like peptide-1 (GLP-1) are hormones released from the gut in response to ingested nutrients, which act on the pancreas to potentiate glucose-induced insulin secretion. These hormones are rapidly inactivated by the circulating enzyme dipeptidyl peptidase IV ([DPIV] CD26). This study describes the effect on glucose tolerance and insulin secretion of inhibiting endogenous DPIV in the rat using Ile-thiazolidide, a specific DPIV inhibitor. High-performance liq. chromatog. (HPLC) anal. of plasma following in vivo administration of 125I-labeled peptides showed that inhibition of DPIV by about 70% prevented the degrdn. of 90.0% of injected 125I-GLP-17-36 after 5 min, while only 13.4% remained unhydrolyzed in rats not treated with the DPIV-inhibiting agent after only 2 min. Ile-thiazolidide treatment also increased the circulating half-life of intact GLP-17-36 released in response to intraduodenal (ID) glucose (as measured by N-terminal specific RIA [RIA]). In addn., inhibition of DPIV in vivo resulted in an earlier

increase and peak of plasma insulin and a more rapid clearance of blood glucose in response to ID glucose challenge. When considered with the HPLC data, these results suggest that the altered insulin profile is an incretin-mediated response. DPIV inhibition resulting in improved glucose tolerance may have therapeutic potential for the management of type 2 **diabetes** mellitus.

IT **136259-20-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(improved glucose tolerance in rats treated with the DPIV inhibitor Ile-thiazolidide)
RN 136259-20-6 HCAPLUS
CN Thiazolidine, 3-[(2S,3S)-2-amino-3-methyl-1-oxopentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(improved glucose tolerance in rats treated with the DPIV **inhibitor** Ile-thiazolidide)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

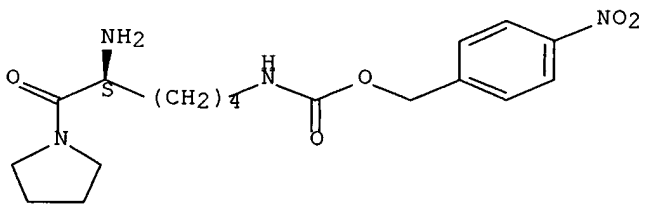
L16 ANSWER 23 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:380796 HCAPLUS
DN 129:135056
TI Inhibitors of dipeptidyl peptidase IV/CD26 suppress activation of human MBP-specific CD4+ T cell clones
AU Reinhold, Dirk; Hemmer, Bernhard; Gran, Bruno; Born, Ilona; Faust, Jurgen; Neubert, Klaus; McFarland, Henry F.; Martin, Roland; Ansorge, Siegfried
CS Department of Internal Medicine, Institute of Experimental Internal Medicine, Otto-von-Guericke-University, Magdeburg, D-39120, Germany
SO J. Neuroimmunol. (1998), 87(1,2), 203-209
CODEN: JNRIDW; ISSN: 0165-5728
PB Elsevier Science B.V.
DT Journal
LA English
AB The ectoenzyme dipeptidyl peptidase IV (DP IV EC 3.4.14.5 CD26) has been shown to play a crucial role in T cell activation. Specific inhibitors of DP IV suppress DNA synthesis as well as cytokine prodn. (IL-2, IL-10, IL-12, IFN-.gamma.) of stimulated human and mouse T cells suggesting a potential application of these effectors in transplantation and autoimmune

diseases. In the present study, the authors have examd. the expression of DP IV/CD26 on six myelin basic protein (MBP)(87-99)-specific, CD4+ T cell clones (TCC) derived from patients with multiple **sclerosis** (MS) as well as the biol. effects of the two synthetic DP IV inhibitors Lys[Z(NO2)]-thiazolidide and Lys[Z(NO2)]-pyrrolidide on the function of these cells. All TCC expressed high levels of DP IV/CD26, as shown by flow cytometry and by enzymic DP IV assay. Enzymic activity of resting TCC was three to fourfold higher than on resting peripheral blood T cells and close to that of T cells 48 h after PHA stimulation. The DP IV inhibitors suppress DNA synthesis and IFN-.gamma., IL-4, and TNF-.alpha. prodn. of the antigen-stimulated TCC. These data suggest that CD26 plays a role in regulation of activation of autoreactive TCC. Further in-vivo investigations, first in exptl. models, will clarify, whether the inhibition of the enzymic activity of DP IV could be a useful tool for therapeutic interventions in MS or other autoimmune diseases.

IT **54249-88-6**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(**inhibitors** of dipeptidyl peptidase IV/CD26 suppress activation of human MBP-specific CD4+ T-cells)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

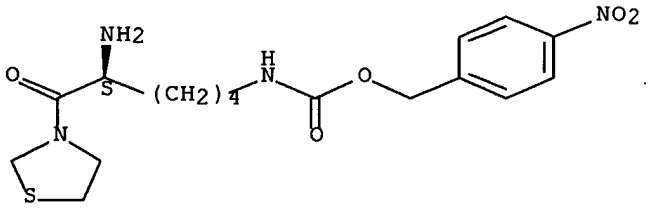
*** STRUCTURE DIAGRAM IS NOT AVAILABLE
IT **136259-18-2 136259-19-3**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(inhibitors of dipeptidyl peptidase IV/CD26 suppress activation of human MBP-specific CD4+ T-cells in relation to)
RN 136259-18-2 HCAPLUS
CN Carbamic acid, [(5S)-5-amino-6-oxo-6-(1-pyrrolidinyl)hexyl]-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



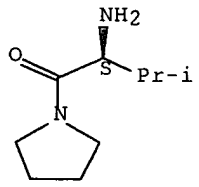
RN 136259-19-3 HCAPLUS
CN Carbamic acid, [(5S)-5-amino-6-oxo-6-(3-thiazolidinyl)hexyl]-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:360329 HCAPLUS
DN 129:90689
TI Dipeptidyl peptidase IV inhibition potentiates the insulinotropic effect of glucagon-like peptide 1 in the anesthetized pig
AU Deacon, Carolyn F.; Hughes, Thomas E.; Holst, Jens J.
CS Department of Medical Physiology, The Panum Institute, University of Copenhagen, Copenhagen N, DK-2200, Den.
SO Diabetes (1998), 47(5), 764-769
CODEN: DIAEAZ; ISSN: 0012-1797
PB American Diabetes Association
DT Journal
LA English
AB Glucagon-like peptide 1 (GLP-1) has been proposed as a new therapeutic agent in the management of **diabetes** because of its glucose-dependent stimulation of insulin secretion, but this is limited by its rapid degrdn. in vivo by dipeptidyl peptidase IV (DPP IV). In nonfasted anesthetized pigs, valine-pyrrolidide (a stable and selective inhibitor of DPP IV), at a dose that reduced plasma DPP IV activity by more than 90%, increased both the amt. of intact GLP-1 in the basal state (from 5 to 18 pM) and the proportion remaining undegraded during an infusion (from 21.0 to 102.3%). This was assocd. with a prolonged plasma half-life for the intact peptide (from 1.0 to 3.2 min). In the basal (nonfasted) state, valine-pyrrolidide potentiated the effect of i.v. GLP-1 on the incremental area under the curve (AUC) for glucose. When an i.v. glucose load was given during the GLP-1 infusion, valine-pyrrolidide augmented the insulin response. These results suggest that by reducing GLP-1 degrdn., DPP IV inhibition potentiates the insulinotropic effect of GLP-1 and may, therefore, be a viable approach to the management of **diabetes**.
IT **54164-07-7**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dipeptidyl peptidase IV inhibition potentiates insulinotropic effect of glucagon-like peptide 1)
RN 54164-07-7 HCAPLUS
CN Pyrrolidine, 1-[(2S)-2-amino-3-methyl-1-oxobutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



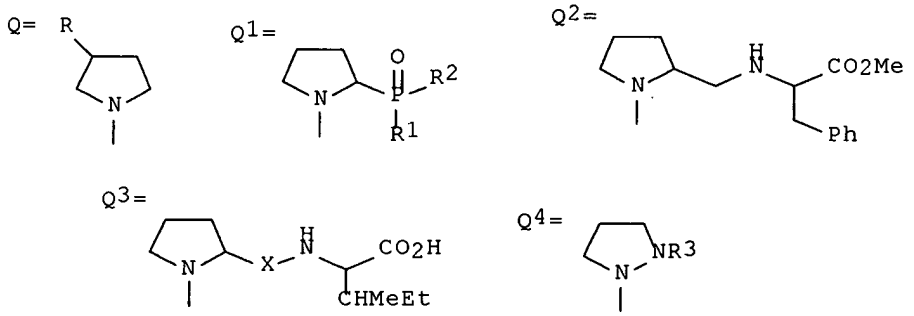
IT **54249-88-6**, Dipeptidyl peptidase IV
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(dipeptidyl peptidase IV **inhibition** potentiates insulinotropic effect of glucagon-like peptide 1)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

L16 ANSWER 25 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:211772 HCAPLUS
DN 124:261758
TI Purification of serine protease and preparation of peptide analogs as inhibitors of serine proteases
IN Augustyns, Koen Jan Ludovicus; Vanhoof, Greta Constantia; Borloo, Marianne Jean Frieda; De, Meester Ingrid Anna Jozef; Goossens, Filip Jozef Anny; Haemers, Achiel Jean-marie; Hendriks, Dirk Frans; Lambeir, Anne-marie Virginie Re; Scharpe, Simon Lodewijk
PA Universitaire Instelling Antwerpen, Belg.
SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9534538	A2	19951221	WO 1995-EP2255	19950609
	WO 9534538	A3	19960215		
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9527908	A1	19960105	AU 1995-27908	19950609
	EP 764151	A2	19970326	EP 1995-923301	19950609
	R: DE, FR, GB				
	US 6090786	A	20000718	US 1997-750484	19970219
PRAI	EP 1994-201668	A	19940610		
	EP 1994-203707	A	19941220		
	WO 1995-EP2255	W	19950609		

OS MARPAT 124:261758
GI



AB New compds. of the general formula R-Xaa-Y1 [Xaa = an amino acid residue selected form Ala, Met, Arg, Phe, Asp, Pro, Asn, Ser, Cys, Thr, Gly, Tyr, Glu, Trp, Gln, Val, Ile, Lys, Leu, L-thioproline, L-homoproline, L-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (Tic), L-2,3-dihydroindole-2-carboxylic acid, L-naphthylglycine, L-phenylglycine, L-phenylproline, O-benzyltyrosine, and .omega.-acetyl-L-lysine; Y1 =

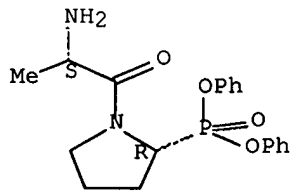
azetidin-1-yl, Q - Q4; wherein R = halo such as Cl or F, :O; R1 = H, C1-4 alkyl, Ph, PhCH2, PhO; R2 = Ph; X = CH2, CH(OH)CH2; R3 = N-alkylcarbamoyl, CONHPh, o- to p-substituted Ph ester such as p-chlorophenyl ester, p-benzoic acid ester, alkoxycarbonyl, phenoxycarbonyl, benzyloxycarbonyl, alkanoyl, COPh, COCH2Ph, CHO, H] or pharmaceutically acceptable salts thereof, which have an inhibitory activity for dipeptidyl peptidase IV (DPPIV) and prolyl oligopeptidase (Pr endopeptidase) and are useful for treating inflammation, vascular diseases, autoimmune disease, multiple **sclerosis**, joint diseases, and diseases assocd. with benign and malign cell transformation, or when optionally labeled, for use in diagnostic methods such as fluorescence and radio assays, imaging, in situ histochem. or cytochem. staining, are prepd. Because of the high specificity of the interaction between adenosine deaminase and DPPIV, a method for purifying DPPIV is developed, involving (1) contacting a DPPIV-contg. ext. with a solid phase material having adenosine deaminase immobilized thereon to bind DPPIV present in the ext., washing the material to remove unbound ext. components, and removal of the DPPIV from the solid phase material. Thus, Z-Pro-OH was coupled with 4-aminobutyraldehyde di-Et acetal using the std. mixed anhydride method with iso-Bu chloroformate to give 92% 4-[(N-benzyloxycarbonyl-L-prolyl)amino]butyraldehyde di-Et acetal as an oil. The latter compd. was treated with HCl in aq. THF at room temp. for 1 h, treated with Et2O, and adjusted to pH 7-8 with 1 N aq. NaOH, followed by sepg. the org. layer an evapg. the solvent to give an oil, which was treated with Ph3P in AcOH at 80-85.degree. for 1 h to give 66% di-Ph 1-[(N-benzyloxycarbonyl-L-prolyl)amino]pyrrolidine-2-phosphate. This compd. was hydrogenolyzed over 10% Pd-C at room temp. for 3-6 h and acidified with HCl in EtOAc/CHCl3 to give di-Ph (S,R)-1-[(S)-prolyl]pyrrolidine-2-phosphate dihydrochloride (I.2HCl). I showed IC50 of 0.07 mM against DPPIV.

IT **161141-08-8P 161141-09-9P 168554-03-8P**
168554-04-9P 168554-05-0P 174298-38-5P
175155-12-1P 175155-13-2P 175155-16-5P
175155-17-6P 175155-18-7P 175155-26-7P
175155-34-7P 175155-35-8P 175155-36-9P
175155-37-0P 175155-38-1P 175155-39-2P
175155-40-5P 175274-86-9P 175274-87-0P
175274-92-7P 175274-93-8P 175274-94-9P
175339-32-9P 175339-33-0P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptide analogs as inhibitors of serine proteases for treating diseases)

RN 161141-08-8 HCAPLUS

CN Phosphonic acid, [1-(2-amino-1-oxopropyl)-2-pyrrolidinyl]-, diphenyl ester, monohydrochloride, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

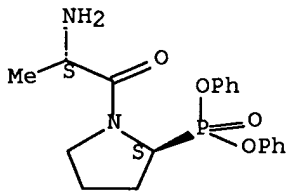
Absolute stereochemistry.



HCl

RN 161141-09-9 HCAPLUS
CN Phosphonic acid, [1-(2-amino-1-oxopropyl)-2-pyrrolidinyl]-, diphenyl ester, monohydrochloride, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

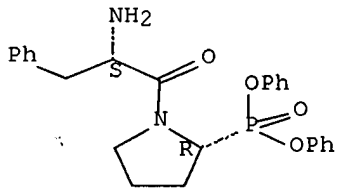
Absolute stereochemistry.



● HCl

RN 168554-03-8 HCAPLUS
CN Phosphonic acid, [1-(2-amino-1-oxo-3-phenylpropyl)-2-pyrrolidinyl]-, diphenyl ester, monohydrochloride, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

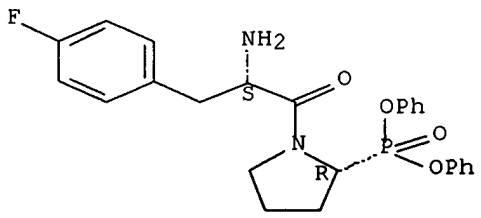
Absolute stereochemistry.



● HCl

RN 168554-04-9 HCAPLUS
CN Phosphonic acid, [1-[2-amino-3-(4-fluorophenyl)-1-oxopropyl]-2-pyrrolidinyl]-, diphenyl ester, monohydrochloride, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

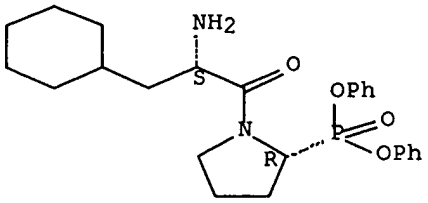
Absolute stereochemistry.



HCl

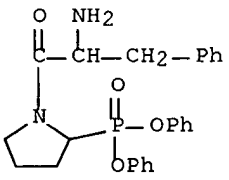
RN 168554-05-0 HCAPLUS
CN Phosphonic acid, [1-(2-amino-3-cyclohexyl-1-oxopropyl)-2-pyrrolidinyl]-, diphenyl ester, monohydrochloride, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



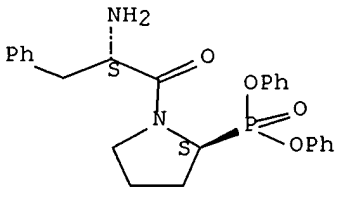
● HCl

RN 174298-38-5 HCAPLUS
CN Phosphonic acid, [1-(2-amino-1-oxo-3-phenylpropyl)-2-pyrrolidinyl]-, diphenyl ester (9CI) (CA INDEX NAME)



RN 175155-12-1 HCAPLUS
CN Phosphonic acid, [1-(2-amino-1-oxo-3-phenylpropyl)-2-pyrrolidinyl]-, diphenyl ester, monohydrochloride, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

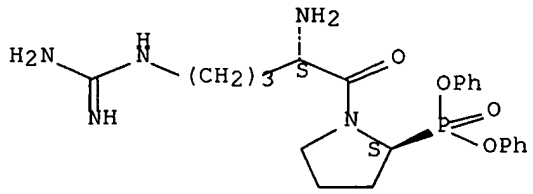
Absolute stereochemistry. Rotation (+).



● HCl

RN 175155-13-2 HCAPLUS
CN Phosphonic acid, [1-[2-amino-5-[(aminoiminomethyl)amino]-1-oxopentyl]-2-pyrrolidinyl]-, diphenyl ester, dihydrochloride, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

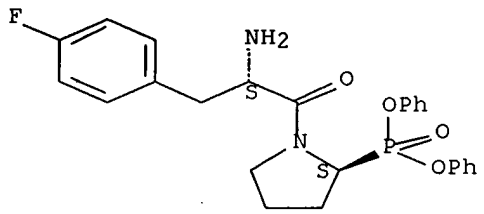
Absolute stereochemistry.



● 2 HCl

RN 175155-16-5 HCAPLUS
CN Phosphonic acid, [1-[2-amino-3-(4-fluorophenyl)-1-oxopropyl]-2-pyrrolidinyl]-, diphenyl ester, monohydrochloride, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

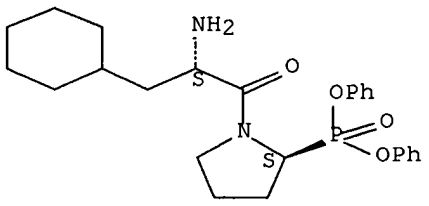
Absolute stereochemistry. Rotation (+).



● HCl

RN 175155-17-6 HCAPLUS
CN Phosphonic acid, [1-(2-amino-3-cyclohexyl-1-oxopropyl)-2-pyrrolidinyl]-, diphenyl ester, monohydrochloride, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

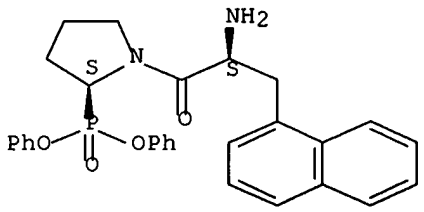
Absolute stereochemistry. Rotation (+).



● HCl

RN 175155-18-7 HCAPLUS
CN Phosphonic acid, [1-[2-amino-3-(1-naphthalenyl)-1-oxopropyl]-2-pyrrolidinyl]-, diphenyl ester, monohydrochloride, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



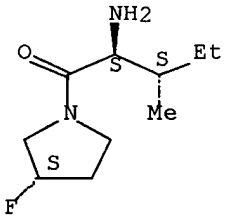
● HCl

RN 175155-26-7 HCAPLUS
CN Pyrrolidine, 1-(2-amino-3-methyl-1-oxopentyl)-3-fluoro-, [3S-[1(2R*,3R*),3R*]]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

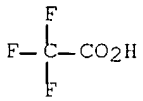
CRN 175155-25-6
CMF C10 H19 F N2 O
CDES *

Absolute stereochemistry.

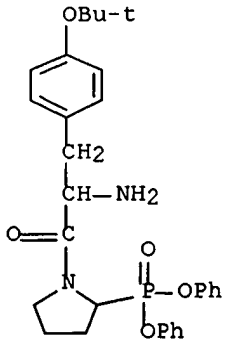


CM 2

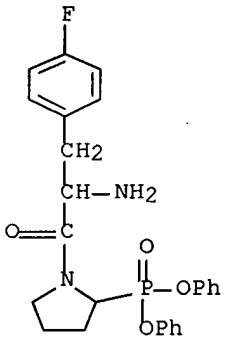
CRN 76-05-1
CMF C2 H F3 O2



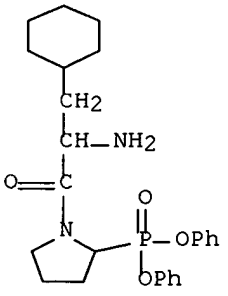
RN 175155-34-7 HCAPLUS
CN Phosphonic acid, [1-[2-amino-3-[4-(1,1-dimethylethoxy)phenyl]-1-oxopropyl]-2-pyrrolidinyl]-, diphenyl ester (9CI) (CA INDEX NAME)



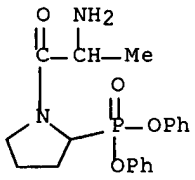
RN 175155-35-8 HCAPLUS
CN Phosphonic acid, [1-[2-amino-3-(4-fluorophenyl)-1-oxopropyl]-2-pyrrolidinyl]-, diphenyl ester (9CI) (CA INDEX NAME)



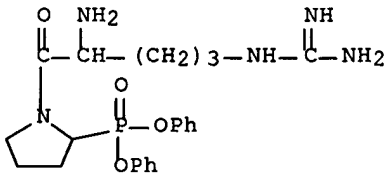
RN 175155-36-9 HCAPLUS
CN Phosphonic acid, [1-(2-amino-3-cyclohexyl-1-oxopropyl)-2-pyrrolidinyl]-, diphenyl ester (9CI) (CA INDEX NAME)



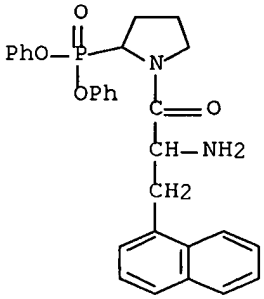
RN 175155-37-0 HCAPLUS
CN Phosphonic acid, [1-(2-amino-1-oxopropyl)-2-pyrrolidinyl]-, diphenyl ester (9CI) (CA INDEX NAME)



RN 175155-38-1 HCAPLUS
CN Phosphonic acid, [1-[2-amino-5-[(aminoiminomethyl)amino]-1-oxopentyl]-2-pyrrolidinyl]-, diphenyl ester (9CI) (CA INDEX NAME)

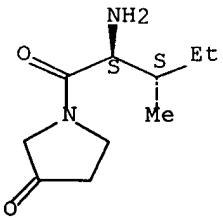


RN 175155-39-2 HCAPLUS
CN Phosphonic acid, [1-[2-amino-3-(1-naphthalenyl)-1-oxopropyl]-2-pyrrolidinyl]-, diphenyl ester (9CI) (CA INDEX NAME)



RN 175155-40-5 HCAPLUS
CN 3-Pyrrolidinone, 1-(2-amino-3-methyl-1-oxopentyl)-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

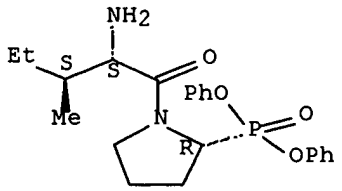
Absolute stereochemistry.



RN 175274-86-9 HCAPLUS

CN Phosphonic acid, [1-(2-amino-3-methyl-1-oxopentyl)-2-pyrrolidinyl]-, diphenyl ester, monohydrochloride, [2R-[1(2S*,3S*),2R*]]- (9CI) (CA INDEX NAME)

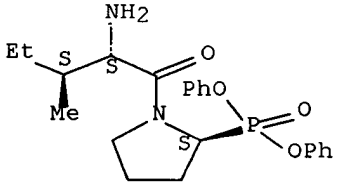
Absolute stereochemistry. Rotation (-).



● HCl

RN 175274-87-0 HCAPLUS
CN Phosphonic acid, [1-(2-amino-3-methyl-1-oxopentyl)-2-pyrrolidinyl]-, diphenyl ester, monohydrochloride, [2S-[1(2R*,3R*),2R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



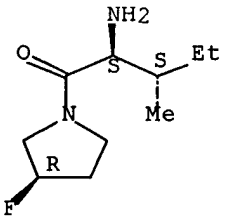
● HCl

RN 175274-92-7 HCAPLUS
CN Pyrrolidine, 1-(2-amino-3-methyl-1-oxopentyl)-3-fluoro-, [3R-[1(2S*,3S*),3R*]]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

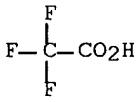
CRN 175274-91-6
CMF C10 H19 F N2 O
CDES *

Absolute stereochemistry.

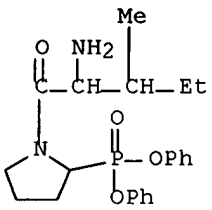


CM 2

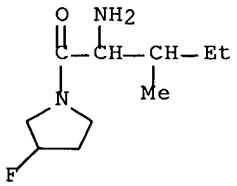
CRN 76-05-1
CMF C2 H F3 O2



RN 175274-93-8 HCAPLUS
CN Phosphonic acid, [1-(2-amino-3-methyl-1-oxopentyl)-2-pyrrolidinyl]-, diphenyl ester (9CI) (CA INDEX NAME)

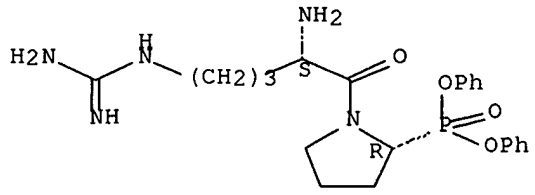


RN 175274-94-9 HCAPLUS
CN Pyrrolidine, 1-(2-amino-3-methyl-1-oxopentyl)-3-fluoro- (9CI) (CA INDEX NAME)



RN 175339-32-9 HCAPLUS
CN Phosphonic acid, [1-[2-amino-5-[(aminoiminomethyl)amino]-1-oxopentyl]-2-pyrrolidinyl]-, diphenyl ester, dihydrochloride, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

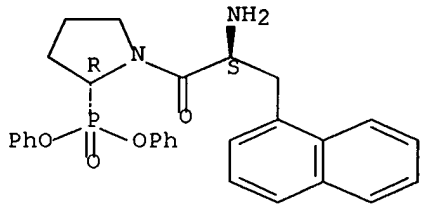
Absolute stereochemistry.



● 2 HCl

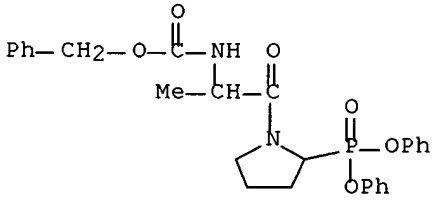
RN 175339-33-0 HCAPLUS
CN Phosphonic acid, [1-[2-amino-3-(1-naphthalenyl)-1-oxopropyl]-2-pyrrolidinyl]-, diphenyl ester, monohydrochloride, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

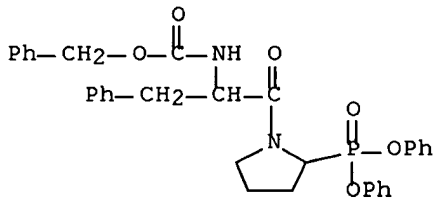


● HCl

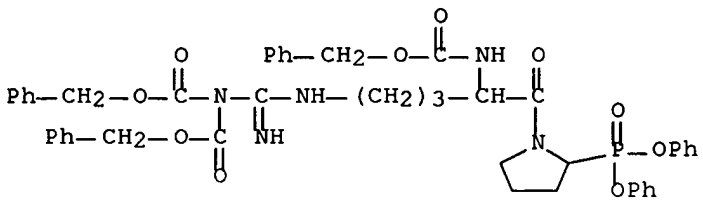
IT **174298-20-5P 174298-27-2P 175155-42-7P**
175155-45-0P 175155-46-1P 175155-47-2P
175155-50-7P 175274-95-0P 175274-97-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of peptide analogs as inhibitors of serine proteases for treating diseases)
RN 174298-20-5 HCAPLUS
CN Carbamic acid, [2-[2-(diphenoxyphosphinyl)-1-pyrrolidinyl]-1-methyl-2-oxoethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



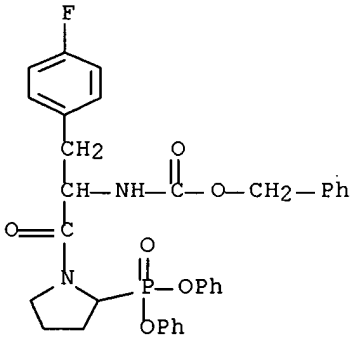
RN 174298-27-2 HCAPLUS
CN Carbamic acid, [2-[2-(diphenoxyphosphinyl)-1-pyrrolidinyl]-2-oxo-1-(phenylmethyl)ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



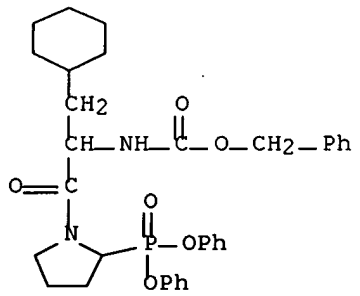
RN 175155-42-7 HCAPLUS
CN 11-Oxa-2,4,9-triazadodecanoic acid, 8-[[2-(diphenoxyphosphinyl)-1-pyrrolidinyl]carbonyl]-3-imino-10-oxo-12-phenyl-2-[(phenylmethoxy)carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



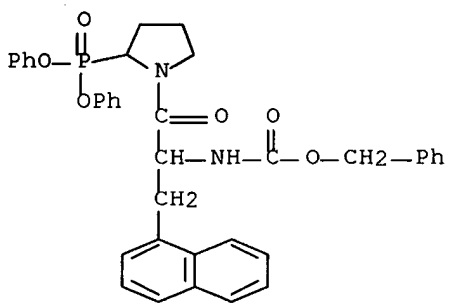
RN 175155-45-0 HCAPLUS
CN Carbamic acid, [2-[2-(diphenoxyphosphinyl)-1-pyrrolidinyl]-1-[(4-fluorophenyl)methyl]-2-oxoethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 175155-46-1 HCAPLUS
CN Carbamic acid, [1-(cyclohexylmethyl)-2-[2-(diphenoxyphosphinyl)-1-pyrrolidinyl]-2-oxoethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

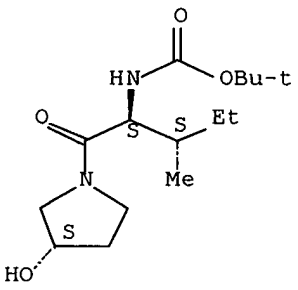


RN 175155-47-2 HCAPLUS
CN Carbamic acid, [2-[2-(diphenoxyphosphinyl)-1-pyrrolidinyl]-1-(1-naphthalenylmethyl)-2-oxoethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

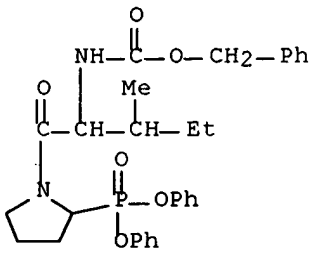


RN 175155-50-7 HCAPLUS
CN Carbamic acid, [1-[(3-hydroxy-1-pyrrolidinyl)carbonyl]-2-methylbutyl]-, 1,1-dimethylethyl ester, [3S-[1(1R*,2R*),3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

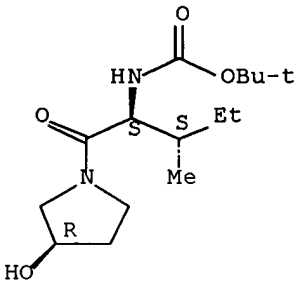


RN 175274-95-0 HCAPLUS
CN Carbamic acid, [1-[[2-(diphenoxyphosphinyl)-1-pyrrolidinyl]carbonyl]-2-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 175274-97-2 HCAPLUS
CN Carbamic acid, [1-[(3-hydroxy-1-pyrrolidinyl)carbonyl]-2-methylbutyl]-, 1,1-dimethylethyl ester, [3R-[1(1S*,2S*),3R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



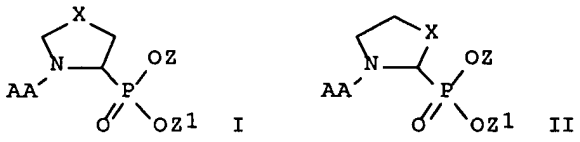
IT **54249-88-6P**, Dipeptidyl peptidase IV
RL: BPR (Biological process); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(purifn. of serine proteases by immobilized adenosine deaminase and prepn. of peptide analogs as **inhibitors** of serine proteases for treating diseases)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

L16 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:153397 HCAPLUS
DN 124:203102
TI Preparation of peptide containing proline phosphonate derivatives as inhibitors of serine proteases
IN Powers, James C.; Boduszek, Bogdan; Oleksyszyn, Jozef
PA Georgia Tech. Research Corp., USA
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9529691	A1	19951109	WO 1995-US5345	19950428
	W: CA, JP, MX				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5543396	A	19960806	US 1994-234181	19940428

PRAI US 1994-234181 19940428
OS MARPAT 124:203102
GI

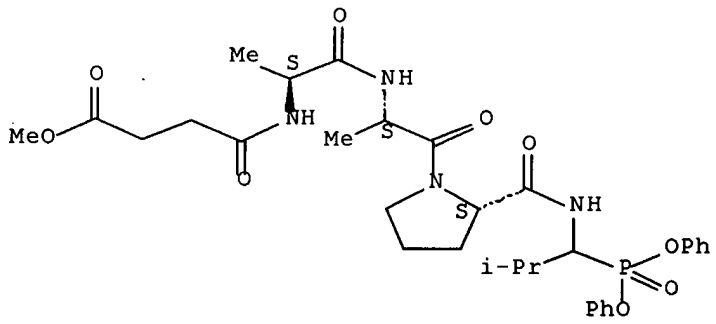


AB Peptidyl derivs. of diesters of .alpha.-aminoalkylphosphonic acids, particularly those with proline or related structures, [I and II; Z, Z1 = C1-6 perfluoroalkyl, (un)substituted Ph; X = a single bond, CH2, CH2CH2, (CH2)3, (CH2)4, Y, CH2Y, YCH2, (H,H); Y = O, S; AA = H, PhCH2O2C, H2NCHRCO (wherein R = C1-6 alkyl optionally fluorinated), .beta.-alanine, glycine, .epsilon.-aminocaproic acid, sarcosine, side chain (un)blocked L-, D-, or DL-.alpha.-amino acid selected from the group consisting of alanine, leucine, isoleucine, proline, methionine, methionine sulfoxide, phenylalanine, tryptophan, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, phenylglycine, and etc.], useful for inhibiting serine proteases with chymotrypsin-like, trypsin-like, elastase-like, and dipeptidyl peptidase IV specificity and their roles as anti-inflammatory agents, anticoagulants, anti-**tumor** agents, and anti-AIDS agents, are prepd. Thus, to 0.36 g Boc-D-Phe-Pro-OH in 2 mL dry DMF at 0.degree., 0.17 g N,N'-dicyclohexylcarbodiimide was added. After stirring the mixt. for 1 h, 0.45 g di-Ph amino(4-amidinophenyl)methanephosphonate dihydrochloride was added the soln. was stirred for 48 h to give di-Ph N-(N-tert-butoxycarbonyl-D-phenylalanyl-L-prolyl)amino(4-amidinophenyl)methanephosphonate hydrochloride. H-Ala-ProP(OC6H4Cl-4)2.HCl and H-Ala-PipP(OC6H4Cl-4)2.HCl in vitro at 0.12 mM inhibited human placenta dipeptidylpeptidase IV (DPP-IV) at 0 and 88% after 2 min, resp., and 88 and 100%, resp., after 30 min.

IT **122299-43-8P 122299-44-9P 130699-15-9P**
130699-16-0P 130727-21-8P 174298-19-2P
174298-20-5P 174298-26-1P 174298-27-2P
174298-28-3P 174298-29-4P 174298-32-9P
174298-33-0P 174298-38-5P 174298-39-6P
174298-41-0P 174391-77-6P 174391-78-7P
174391-79-8P 174391-80-1P 174391-81-2P
174391-82-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptide contg. proline phosphonate derivs. as inhibitors of serine proteases for therapeutics)

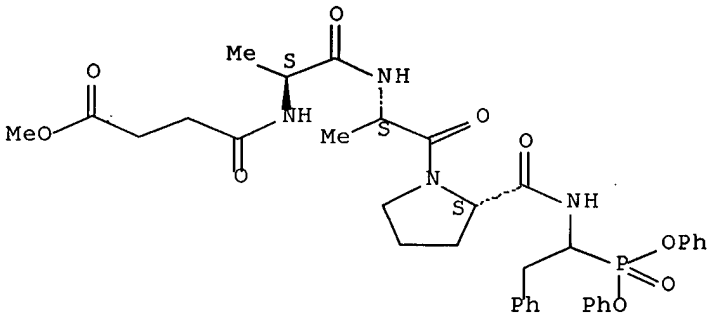
RN 122299-43-8 HCAPLUS
CN L-Prolinamide, N-(4-methoxy-1,4-dioxobutyl)-L-alanyl-L-alanyl-N-[1-(diphenoxyphosphinyl)-2-methylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



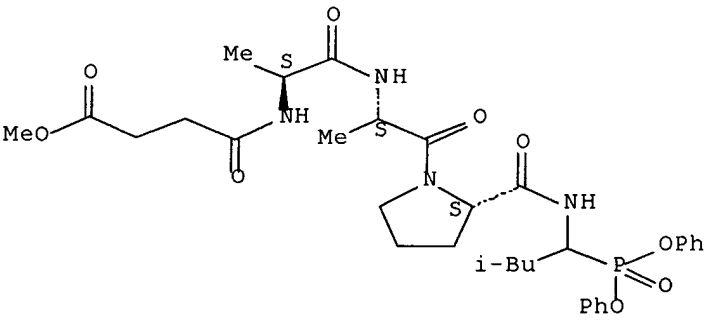
RN 122299-44-9 HCAPLUS
CN L-Prolinamide, N-(4-methoxy-1,4-dioxobutyl)-L-alanyl-L-alanyl-N-[1-(diphenoxyphosphinyl)-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



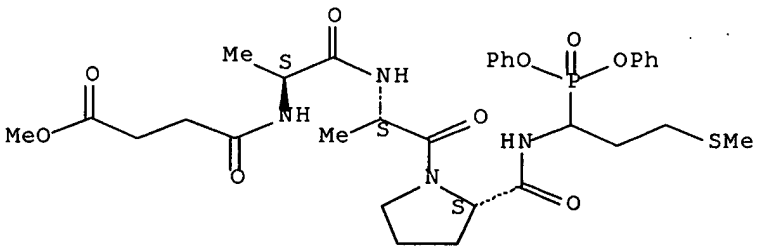
RN 130699-15-9 HCAPLUS
CN L-Prolinamide, N-(4-methoxy-1,4-dioxobutyl)-L-alanyl-L-alanyl-N-[1-(diphenoxyphosphinyl)-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



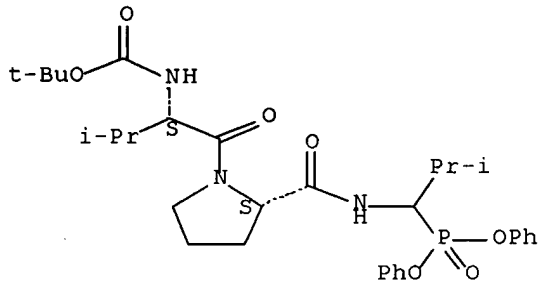
RN 130699-16-0 HCAPLUS
CN L-Prolinamide, N-(4-methoxy-1,4-dioxobutyl)-L-alanyl-L-alanyl-N-[1-(diphenoxyphosphinyl)-3-(methylthio)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

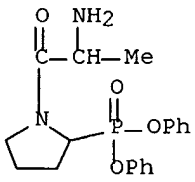


RN 130727-21-8 HCAPLUS
CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-valyl-N-[1-(diphenoxyphosphinyl)-2-methylpropyl]- (9CI) (CA INDEX NAME)

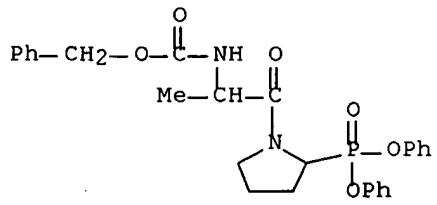
Absolute stereochemistry.



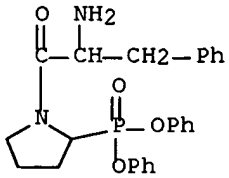
RN 174298-19-2 HCAPLUS
CN Phosphonic acid, [1-(2-amino-1-oxopropyl)-2-pyrrolidinyl]-, diphenyl ester, monohydrochloride (9CI) (CA INDEX NAME)



RN 174298-20-5 HCAPLUS
CN Carbamic acid, [2-[2-(diphenoxyphosphinyl)-1-pyrrolidinyl]-1-methyl-2-oxoethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

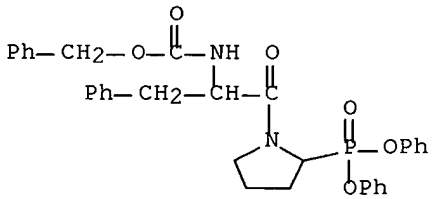


RN 174298-26-1 HCAPLUS
CN Phosphonic acid, [1-(2-amino-1-oxo-3-phenylpropyl)-2-pyrrolidinyl]-, diphenyl ester, monohydrobromide (9CI) (CA INDEX NAME)

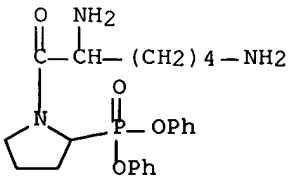


● HBr

RN 174298-27-2 HCAPLUS
CN Carbamic acid, [2-[2-(diphenoxyphosphinyl)-1-pyrrolidinyl]-2-oxo-1-(phenylmethyl)ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

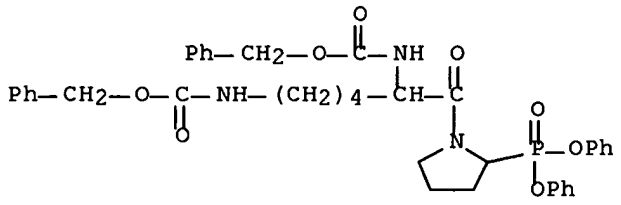


RN 174298-28-3 HCAPLUS
CN Phosphonic acid, [1-(2,6-diamino-1-oxohexyl)-2-pyrrolidinyl]-, diphenyl ester, dihydrobromide (9CI) (CA INDEX NAME)

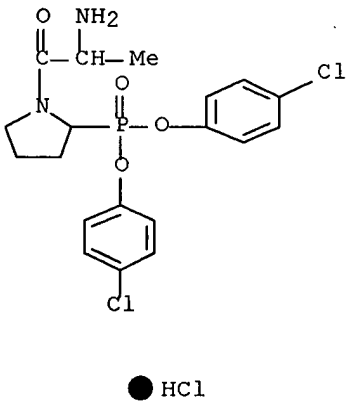


2 HBr

RN 174298-29-4 HCAPLUS
CN Carbamic acid, [1-[[2-(diphenoxyphosphinyl)-1-pyrrolidinyl]carbonyl]-1,5-pentanediyl]bis-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

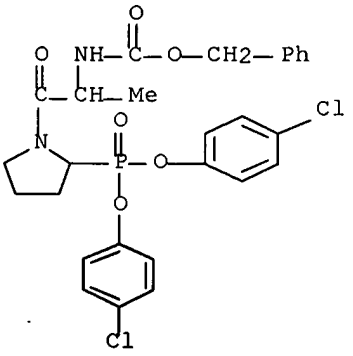


RN 174298-32-9 HCAPLUS
CN Phosphonic acid, [1-(2-amino-1-oxopropyl)-2-pyrrolidinyl]-, bis(4-chlorophenyl) ester, monohydrochloride (9CI) (CA INDEX NAME)



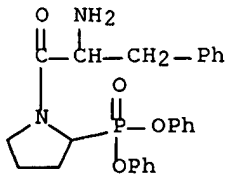
● HCl

RN 174298-33-0 HCAPLUS
CN Carbamic acid, [2-[2-[bis(4-chlorophenoxy)phosphinyl]-1-pyrrolidinyl]-1-methyl-2-oxoethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

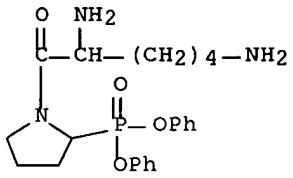


RN 174298-38-5 HCAPLUS

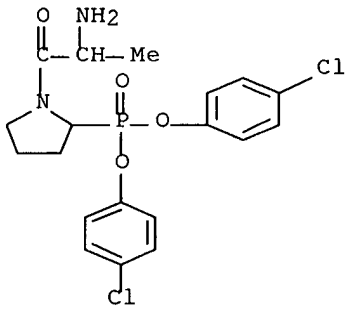
CN Phosphonic acid, [1-(2-amino-1-oxo-3-phenylpropyl)-2-pyrrolidinyl]-, diphenyl ester (9CI) (CA INDEX NAME)



RN 174298-39-6 HCAPLUS
CN Phosphonic acid, [1-(2,6-diamino-1-oxohexyl)-2-pyrrolidinyl]-, diphenyl ester (9CI) (CA INDEX NAME)

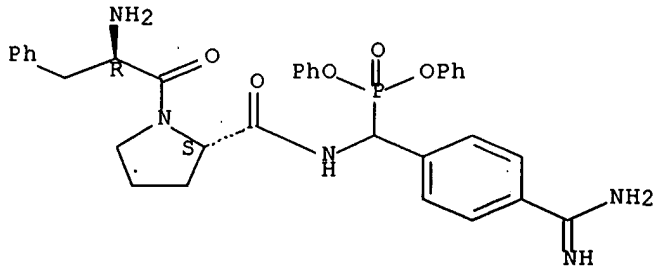


RN 174298-41-0 HCAPLUS
CN Phosphonic acid, [1-(2-amino-1-oxopropyl)-2-pyrrolidinyl]-, bis(4-chlorophenyl) ester (9CI) (CA INDEX NAME)



RN 174391-77-6 HCAPLUS
CN L-Prolinamide, D-phenylalanyl-N-[[4-(aminoiminomethyl)phenyl](diphenoxyphosphinyl)methyl]-, dihydrochloride (9CI) (CA INDEX NAME)

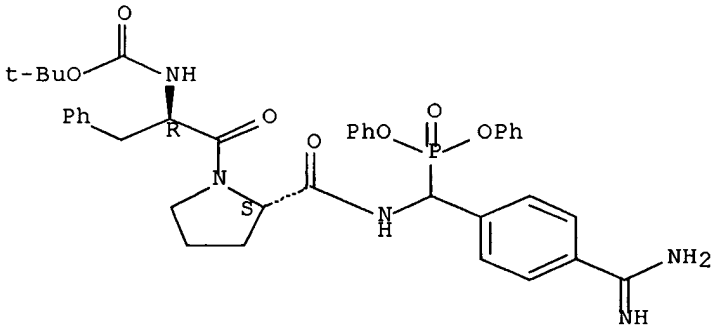
Absolute stereochemistry.



●2 HCl

RN 174391-78-7 HCAPLUS
CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-D-phenylalanyl-N-[[4-(aminoiminomethyl)phenyl](diphenoxyphosphinyl)methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

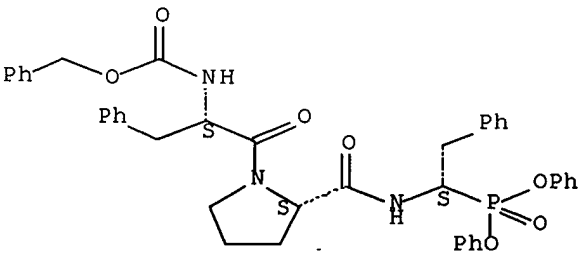
Absolute stereochemistry.



● HCl

RN 174391-79-8 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N-[1-(diphenoxyphosphinyl)-2-phenylethyl]-, (S)- (9CI) (CA INDEX NAME)

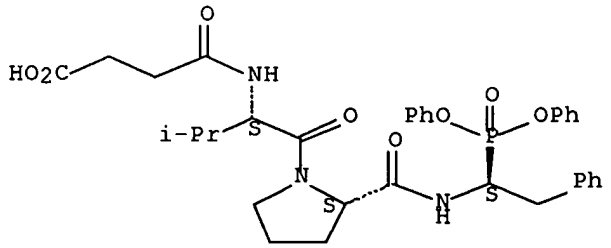
Absolute stereochemistry.



RN 174391-80-1 HCAPLUS
CN L-Prolinamide, N-(3-carboxy-1-oxopropyl)-L-valyl-N-[(1S)-1-

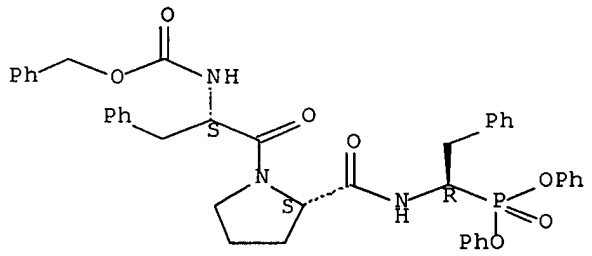
(diphenoxyphosphinyl)-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



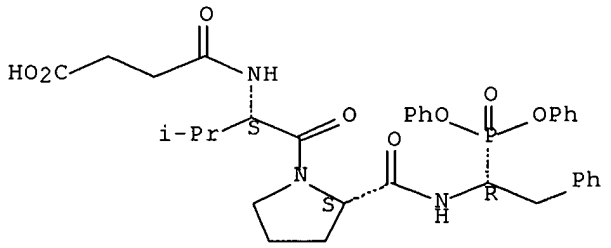
RN 174391-81-2 HCAPLUS
CN L-Prolinamide, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N-[1-(diphenoxyphosphinyl)-2-phenylethyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 174391-82-3 HCAPLUS
CN L-Prolinamide, N-(3-carboxy-1-oxopropyl)-L-valyl-N-[(1R)-1-(diphenoxyphosphinyl)-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



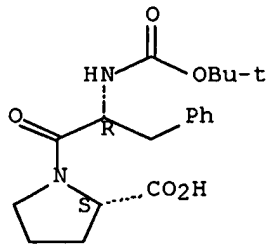
IT **54249-88-6**, Dipeptidylpeptidase IV
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prepn. of peptide contg. proline phosphonate derivs. as **inhibitors** of serine proteases for therapeutics)
RN 54249-88-6 HCAPLUS
CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE
IT **38675-10-4 72252-95-0**

RL: RCT (Reactant)
(prepn. of peptide contg. proline phosphonate derivs. as inhibitors of serine proteases for therapeutics)

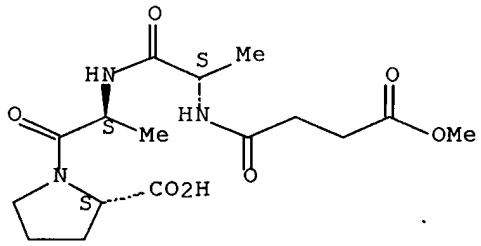
RN 38675-10-4 HCAPLUS
CN L-Proline, N-[(1,1-dimethylethoxy)carbonyl]-D-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 72252-95-0 HCAPLUS
CN L-Proline, 1-[N-[N-(4-methoxy-1,4-dioxobutyl)-L-alanyl]-L-alanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:136508 HCAPLUS
DN 124:224668
TI Prolyl endopeptidase inhibitory activity of a glial fibrillary acidic protein fragment and other proline-rich peptides
AU Maruyama, Susumu; Ohmori, Takashi; Nakagami, Tatsuyoshi
CS Natl. Inst. Biosci. Hum. Technol., Agency Ind. Sci. Technol., Tsukuba, 305, Japan
SO Biosci., Biotechnol., Biochem. (1996), 60(2), 358-9
CODEN: BBBIEJ; ISSN: 0916-8451
DT Journal
LA English
AB The bovine **brain** prolyl endopeptidase (I)-inhibitory activity of synthetic peptides related to the bovine **brain**-derived I inhibitor, glial fibrillary acidic protein (GFAP)-(38-55) (MPPPLPARVDFSLAGALN), was investigated. Homologous peptides, such as MPPPLPTRVDFSLAGALN (human type) and MTPPLPARVDFSLAGALN (mouse type), also inhibited I. Among various synthetic fragments of GFAP-(38-55), only MPPPLP had a Ki essentially the same as that of GFAP-(38-55). Similar synthetic proline-rich peptides, such as synapsin fragments and SH3 domain-binding peptides, had more or less inhibitory activity. The

inhibitory activity of some of these peptides on another member of the prolyl oligopeptidase family, dipeptidyl aminopeptidase IV, was also studied and compared with their effects on I.

IT **54249-88-6**, Dipeptidyl aminopeptidase IV
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(dipeptidyl aminopeptidase IV-**inhibitory** activity of proline-rich peptides)

RN 54249-88-6 HCAPLUS

CN Peptidase, dipeptidyl, IV (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

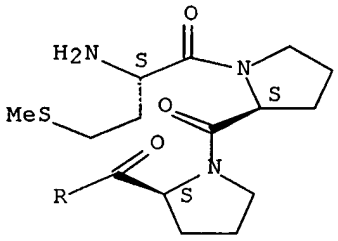
IT **157079-67-9 172515-02-5 174753-60-7**
174753-61-8 174753-62-9 174753-63-0
174753-64-1 174753-65-2 174753-66-3
174753-67-4 174753-68-5 174753-69-6
174753-70-9
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study)
(prolyl endopeptidase-inhibitory activity of glial fibrillary acidic protein-related peptides and other proline-rich peptides)

RN 157079-67-9 HCAPLUS

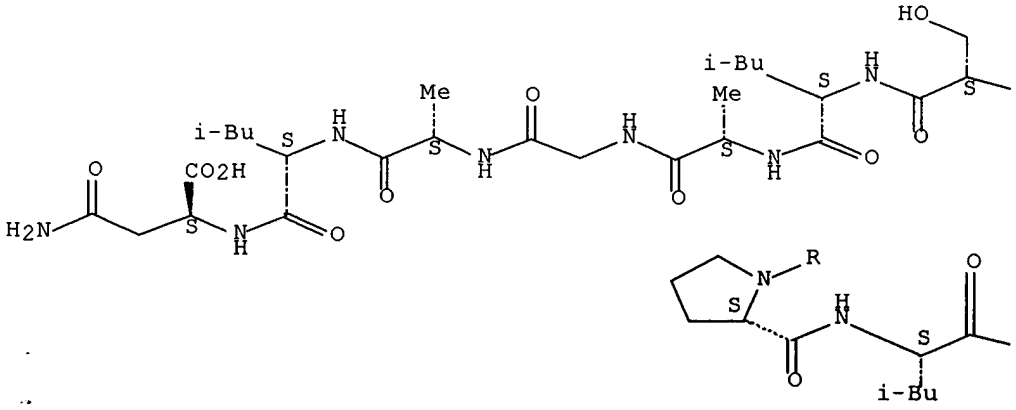
CN L-Asparagine, L-methionyl-L-prolyl-L-prolyl-L-prolyl-L-leucyl-L-prolyl-L-alanyl-L-arginyl-L-valyl-L-.alpha.-aspartyl-L-phenylalanyl-L-seryl-L-leucyl-L-alanylglycyl-L-alanyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

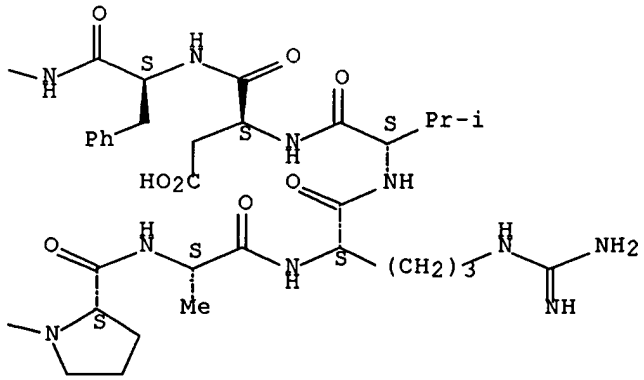
PAGE 1-A



PAGE 2-A



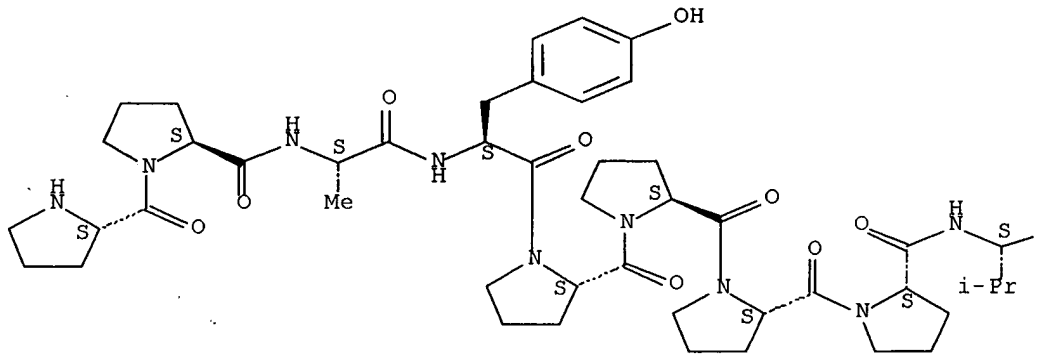
PAGE 2-B



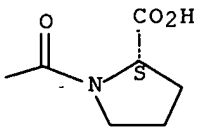
RN 172515-02-5 HCAPLUS
CN L-Proline, L-prolyl-L-prolyl-L-alanyl-L-tyrosyl-L-prolyl-L-prolyl-L-prolyl-L-prolyl-L-valyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

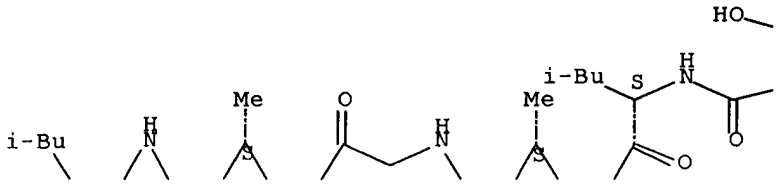


RN 174753-60-7 HCAPLUS

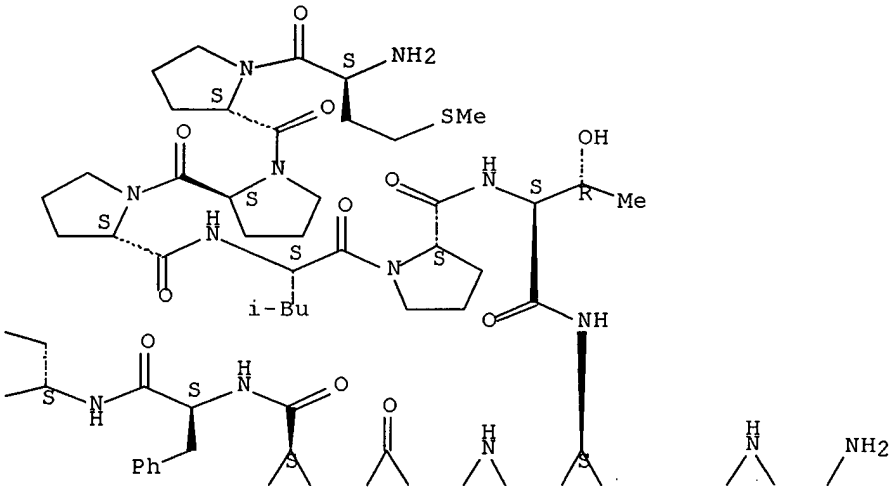
CN L-Asparagine, L-methionyl-L-prolyl-L-prolyl-L-prolyl-L-leucyl-L-prolyl-L-threonyl-L-arginyl-L-valyl-L-.alpha.-aspartyl-L-phenylalanyl-L-seryl-L-leucyl-L-alanylglycyl-L-alanyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

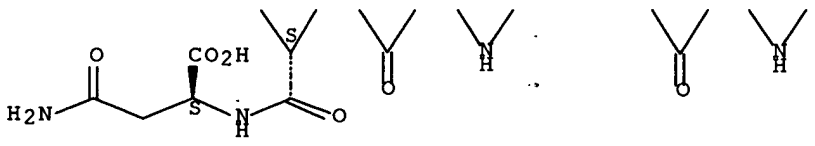
PAGE 1-A



PAGE 1-B



PAGE 2-A

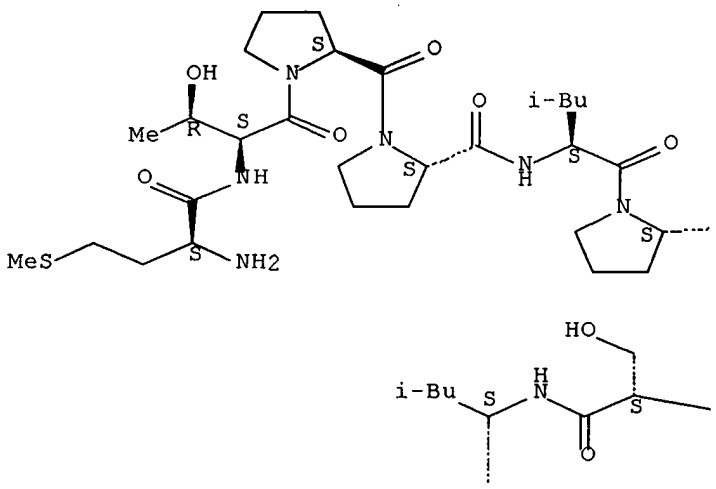


PAGE 2-B

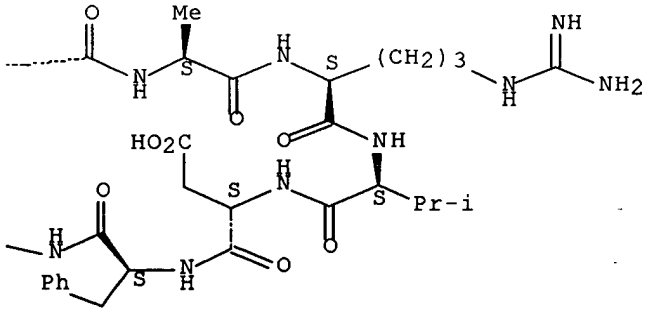
RN 174753-61-8 HCAPLUS
CN L-Asparagine, L-methionyl-L-threonyl-L-prolyl-L-prolyl-L-leucyl-L-prolyl-L-alanyl-L-arginyl-L-valyl-L-.alpha.-aspartyl-L-phenylalanyl-L-seryl-L-leucyl-L-alanylglycyl-L-alanyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

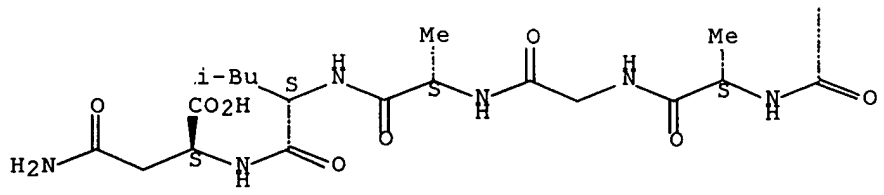
PAGE 1-A



PAGE 1-B

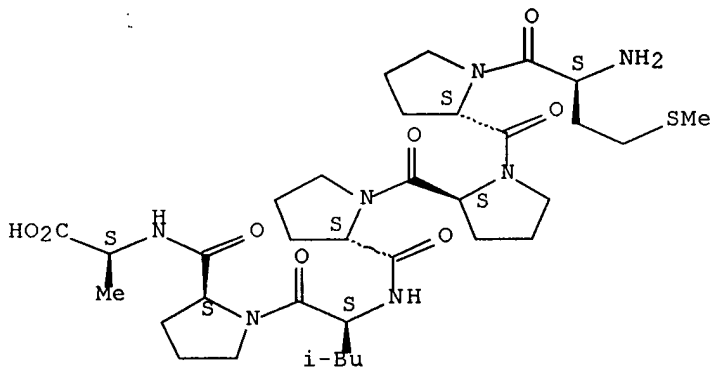


PAGE 2-A



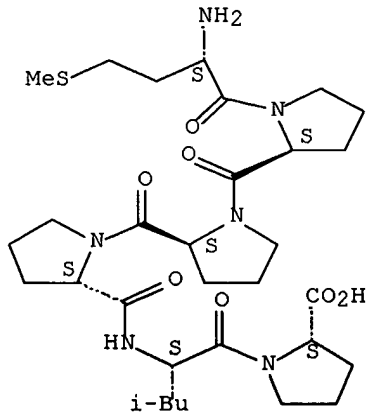
RN 174753-62-9 HCAPLUS
CN L-Alanine, L-methionyl-L-prolyl-L-prolyl-L-prolyl-L-leucyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 174753-63-0 HCAPLUS
CN L-Proline, L-methionyl-L-prolyl-L-prolyl-L-prolyl-L-leucyl- (9CI) (CA INDEX NAME)

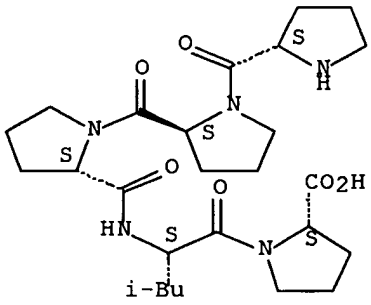
Absolute stereochemistry.



RN 174753-64-1 HCAPLUS

CN L-Proline, 1-[N-[1-(1-L-prolyl-L-prolyl)-L-prolyl]-L-leucyl]- (9CI) (CA INDEX NAME)

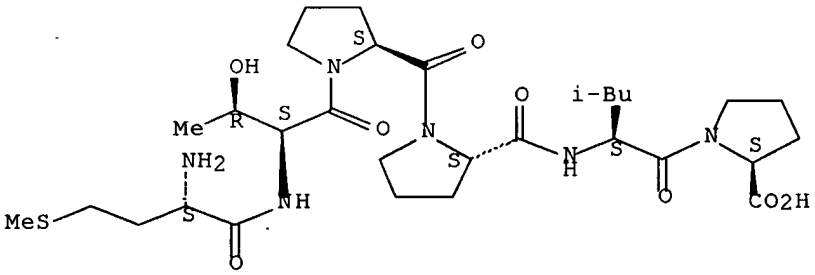
Absolute stereochemistry.



RN 174753-65-2 HCAPLUS

CN L-Proline, 1-[N-[1-[1-(N-L-methionyl-L-threonyl)-L-prolyl]-L-prolyl]-L-leucyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

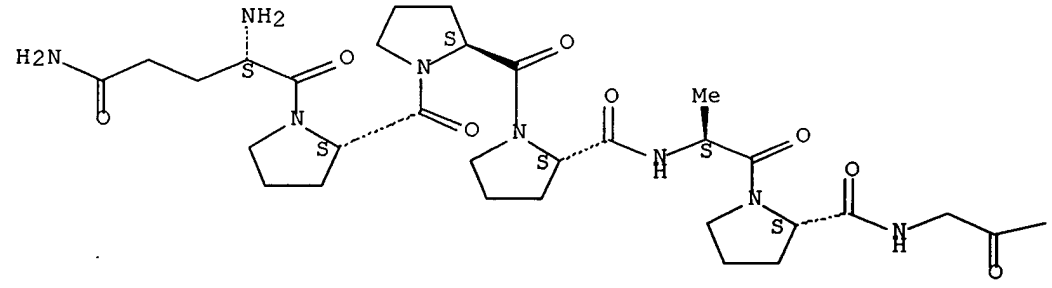


RN 174753-66-3 HCAPLUS

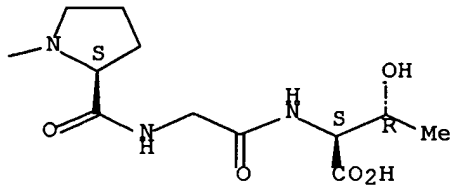
CN L-Threonine, N-[N-[1-[N-[1-[N-[1-[1-(1-L-glutaminyl-L-prolyl)-L-prolyl]-L-prolyl]-L-alanyl]-L-prolyl]glycyl]-L-prolyl]glycyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



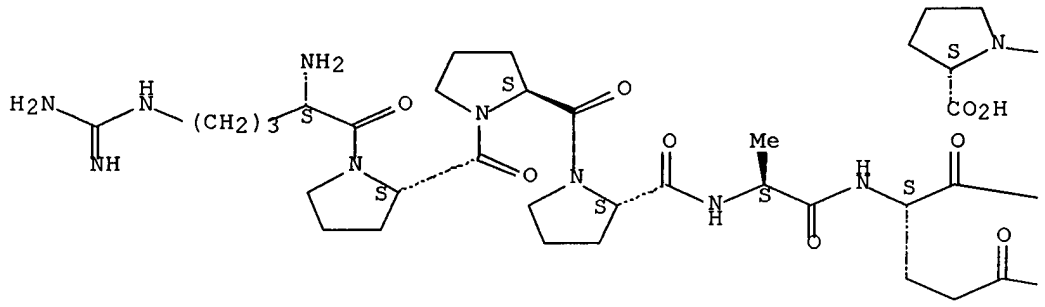
PAGE 1-B



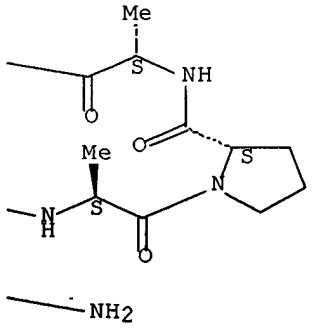
RN 174753-67-4 HCAPLUS
CN L-Proline, 1-[N-[1-[N-[N2-[N-[1-[1-(1-L-arginyl-L-prolyl)-L-prolyl]-L-prolyl]-L-alanyl]-L-glutaminyl]-L-alanyl]-L-prolyl]-L-alanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



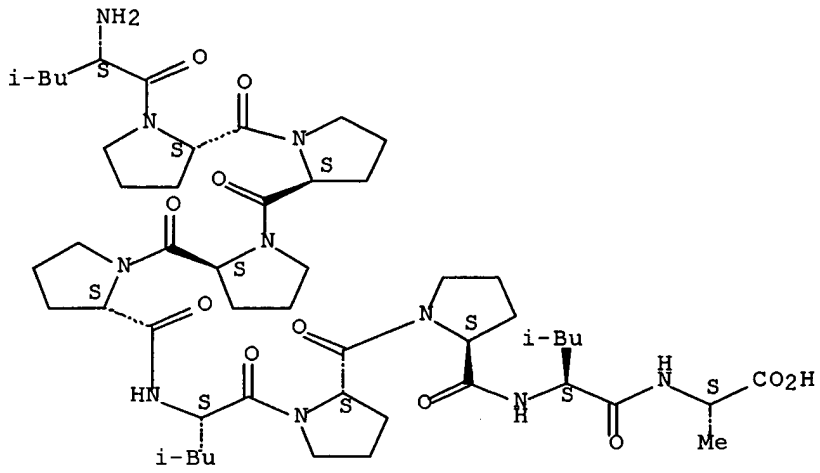
PAGE 1-B



RN 174753-68-5 HCAPLUS

CN L-Alanine, N-[N-[1-[1-[N-[1-[1-[1-(1-L-leucyl-L-prolyl)-L-prolyl]-L-prolyl]-L-prolyl]-L-leucyl]-L-prolyl]-L-prolyl]-L-leucyl]- (9CI) (CA INDEX NAME)

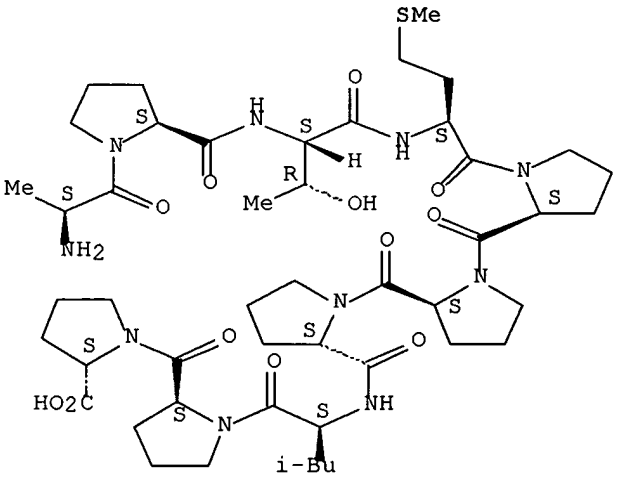
Absolute stereochemistry.



RN 174753-69-6 HCAPLUS

CN L-Proline, L-alanyl-L-prolyl-L-threonyl-L-methionyl-L-prolyl-L-prolyl-L-prolyl-L-leucyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

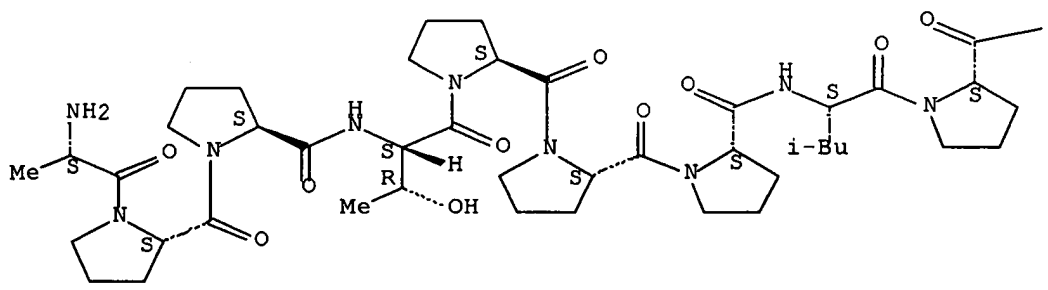


RN 174753-70-9 HCAPLUS

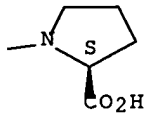
CN L-Proline, 1-[1-[N-[1-[1-[1-[N-[1-(1-L-alanyl-L-prolyl)-L-prolyl]-L-threonyl]-L-prolyl]-L-prolyl]-L-prolyl]-L-leucyl]-L-prolyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

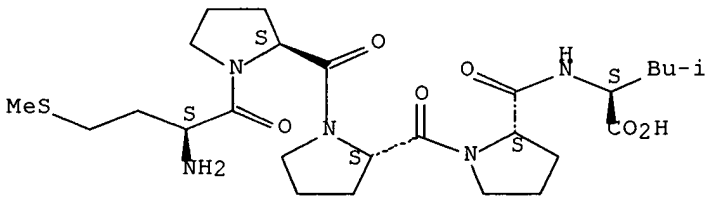


IT **174753-71-0 174753-72-1 174753-73-2**
174753-74-3 174753-75-4 174753-76-5
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(prolyl endopeptidase-inhibitory activity of glial fibrillary acidic protein-related peptides and other proline-rich peptides)

RN 174753-71-0 HCAPLUS

CN L-Leucine, L-methionyl-L-prolyl-L-prolyl-L-prolyl- (9CI) (CA INDEX NAME)

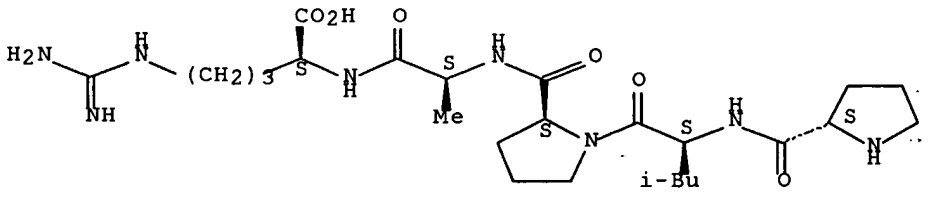
Absolute stereochemistry.



RN 174753-72-1 HCAPLUS

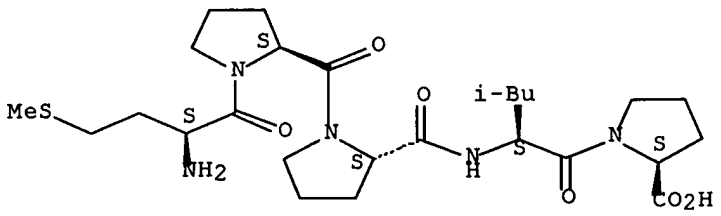
CN L-Arginine, N2-[N-[1-(N-L-prolyl-L-leucyl)-L-prolyl]-L-alanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



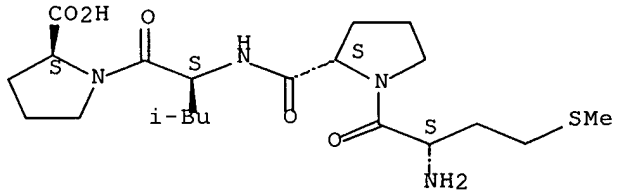
RN 174753-73-2 HCAPLUS
CN L-Proline, 1-[N-[1-(1-L-methionyl-L-prolyl)-L-prolyl]-L-leucyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



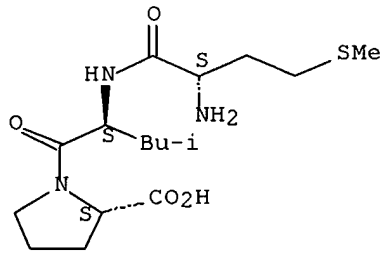
RN 174753-74-3 HCAPLUS
CN L-Proline, 1-[N-(1-L-methionyl-L-prolyl)-L-leucyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



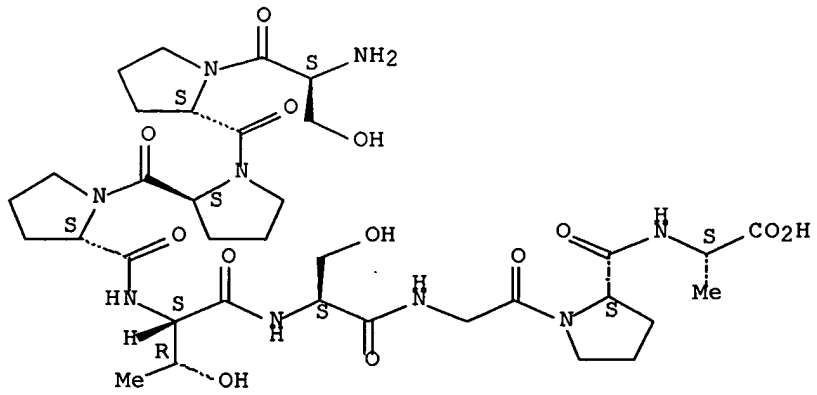
RN 174753-75-4 HCAPLUS
CN L-Proline, 1-(N-L-methionyl-L-leucyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



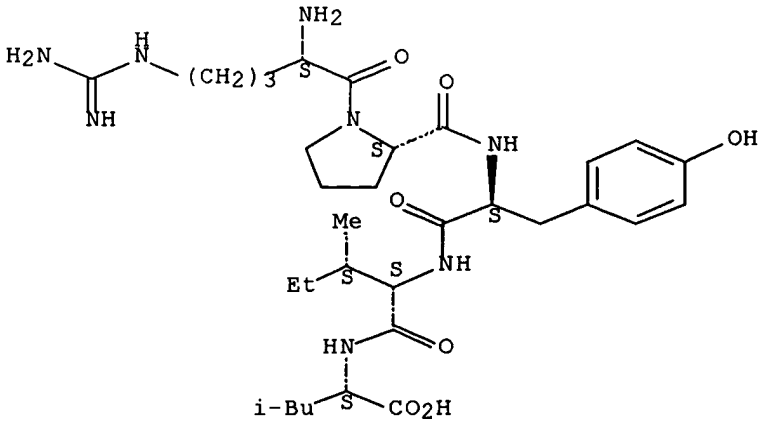
RN 174753-76-5 HCAPLUS
CN L-Alanine, N-[1-[N-[N-[N-[1-[1-(1-L-seryl-L-prolyl)-L-prolyl]-L-prolyl]-L-threonyl]-L-seryl]glycyl]-L-prolyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 28 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 1987:132126 HCAPLUS
DN 106:132126
TI Catabolism of neurotensin by neural (neuroblastoma clone N1E115) and extraneural (HT29) cell lines
AU Checler, Frederic; Amar, Shimon; Kitabgi, Patrick; Vincent, Jean Pierre
CS Cent. Biochim., Univ. Nice, Nice, 06034, Fr.
SO Peptides (Fayetteville, N. Y.) (1986), 7(6), 1071-7
CODEN: PPTDD5; ISSN: 0196-9781
DT Journal
LA English
AB The mechanisms by which neurotensin (NT) [39379-15-2] was inactivated by differentiated neuroblastoma and HT29 cells were characterized. In both cell lines, the sites of primary cleavages of NT were Pro7-Arg8, Arg8-Arg8, and Pro10-Tyr11 bonds. The cleavage at the Pro7-Arg8 bond was totally **inhibited** by N-benzyloxycarbonyl-prolyl-prolinal and therefore resulted from the action of proline endopeptidase [72162-84-6]. This peptidase also contributed in a major way to the cleavage at the Pro10-Tyr11 bond. However, the latter breakdown was partly due to an NT-degrading neurotensin metalloendopeptidase [90463-53-9]. The involvement of a rat **brain** metalloendopeptidase [80498-19-7] at the Arg8-Arg9 site was demonstrated using its specific **inhibitor** N-[1(R,S)-carboxy-2-phenylethyl]-alanylalanylphenylalanine-p-aminobenzoate. The secondary processing of NT degrdn. products revealed differences between HT29 and N1E115 cells. Angiotensin-converting enzyme [9015-82-1] degraded NT1-10 [**63524-00-5**] and NT1-7 [**82882-13-1**] in N1E115 cells but was not detected in HT29 cells. A post-proline dipeptidyl aminopeptidase [**67339-10-0**] activity converted NT9-13 [**60482-96-4**] into NT11-13 [60482-98-6] in HT29 cells but not in N1E115 cells. Finally bestatin-sensitive aminopeptidases rapidly broke down NT11-13 to Tyr in both cell lines. Models for the inactivation of NT in HT29 and N1E115 cells are proposed and compared to that previously described for purified rat **brain** synaptic membranes.
IT **60482-96-4**, Neurotensin 9-13 **63524-00-5** **82882-13-1**
RL: PRP (Properties)
(degrdn. of, in neural and extraneural cell lines)
RN 60482-96-4 HCAPLUS
CN L-Leucine, L-arginyl-L-prolyl-L-tyrosyl-L-isoleucyl- (9CI) (CA INDEX NAME)

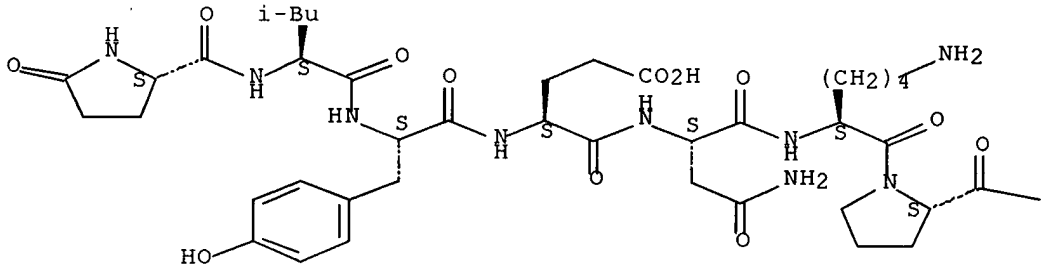
Absolute stereochemistry.



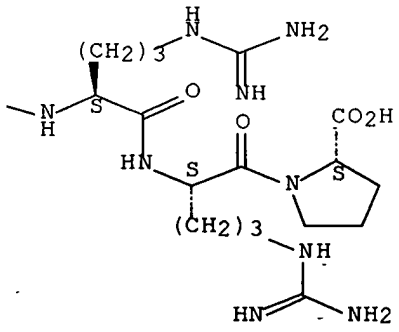
RN 63524-00-5 HCAPLUS
CN 1-10-Neurotensin (cattle) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



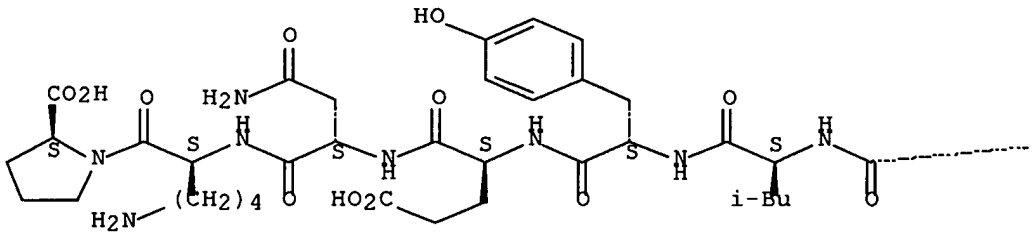
PAGE 1-B



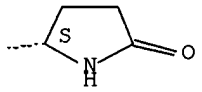
RN 82882-13-1 HCAPLUS
CN 1-7-Neurotensin (cattle) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

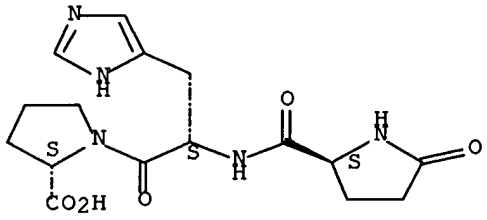


L16 ANSWER 29 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 1985:432505 HCAPLUS
DN 103:32505
TI Metabolism of thyrotropin releasing hormone and its possible relevance to prolactin secretion
AU Charli, Jean Louis; Garat, Beatriz; Martinez-Escalera, Gonzalo; Ponce, Georgina; Miranda, Juan; Joseph-Bravo, Patricia
CS Cent. Invest. Ing. Genet. Biotecnol., Univ. Nac. Auton. Mexico, Mexico City, 04510, Mex.
SO Prolactin Secretion, [Proc. Symp. Front. Perspect. Prolactin Secretion] (1984), Meeting Date 1982, 239-48. Editor(s): Mena, Flavio; Valverde-R., Carlos. Publisher: Academic, Orlando, Fla.
CODEN: 53OWAI
DT Conference
LA English
AB The TRH [**24305-27-9**] metabolite, His-Pro-diketopiperazine (HP-DKP) [53109-32-3], **inhibited** release of both mature and newly formed prolactin [9002-62-4] by rat adenohypophysis in vitro. [3H]TRH was accumulated by hypothalamic slices in a time- and temp.-dependent manner. The saturable part of accumulation was **inhibited** by ouabain, dinitrophenol, and the absence of glucose, suggesting an uptake process similar to those inactivating some neurotransmitters. TRH-OH [**24769-58-2**] and HP-DKP were found in the sol. supernatant of rat **brain** homogenized under conditions preserving pyroglutamidase [9075-21-2] and post-proline-cleaving enzyme [72162-84-6]. Moreover, **brain** membrane contained a pyroglutamidase which differs from the sol. enzyme but is similar to serum thyroliberinase. **Brain** slices and membrane fractions also contained an imidopeptidase [70712-47-9] and

post-proline dipeptiylaminopeptidase [**67339-10-0**] which are important in the metab. of His-Pro-NH2 [**33605-69-5**] and HP-DKP. Results are discussed in relation to the effects of HP-DKP on prolactin metab. as well as the pathway of the enzyme formation.

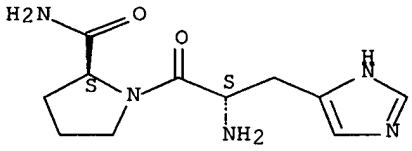
IT **24769-58-2**
RL: BIOL (Biological study)
(as TRH metabolite, in **brain**)
RN 24769-58-2 HCAPLUS
CN L-Proline, 5-oxo-L-prolyl-L-histidyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



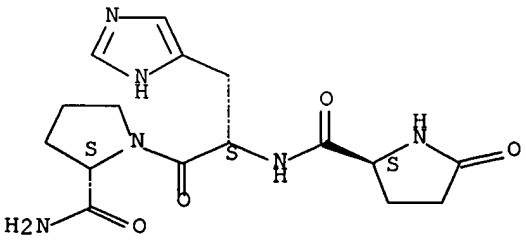
IT **33605-69-5**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metab. of, by **brain**, enzymes in relation to)
RN 33605-69-5 HCAPLUS
CN L-Prolinamide, L-histidyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **24305-27-9**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metab. of, by **brain**, prolactin secretion in relation to)
RN 24305-27-9 HCAPLUS
CN L-Prolinamide, 5-oxo-L-prolyl-L-histidyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2002 ACS
AN 1985:56646 HCAPLUS
DN 102:56646
TI Degradation of substance P by neurons and glial cells
AU Horsthemke, Bernhard; Schulz, Michael; Bauer, Karl
CS Inst. Biochem. Mol. Biol., Tech. Univ., Berlin, D-1000/10, Fed. Rep. Ger.
SO Biochem. Biophys. Res. Commun. (1984), 125(2), 728-33
CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
AB Neuronal and astroblast-rich cultures from rat **brain** degrade exogenously added substance P [**33507-63-0**]. The rate of degrdn. is decreased by diisopropyl fluorophosphate (DFP), phosphoramidon, and bacitracin, but not by N-ethylmaleimide or bestatin. When DFP, phosphoramidon, and bacitracin are simultaneously present in the culture medium, the degrdn. of substance P is completely **inhibited.** Apparently, the hydrolysis of substance P by intact cells is catalyzed by a postproline dipeptidylaminopeptidase [**67339-10-0**], a thermolysinlike metalloproteinase [80498-20-0], and a yet uncharacterized bacitracin-sensitive enzyme activity. Although the thermolysinlike metalloproteinase activity is mainly assocd. with glial cells, the specific activities of the outer enzymes are 5-fold higher in the neuronal culture.
IT **33507-63-0**
RL: PRP (Properties)
(degrdn. of, by glial cells and neurons, enzymes in)
RN 33507-63-0 HCAPLUS
CN Substance P (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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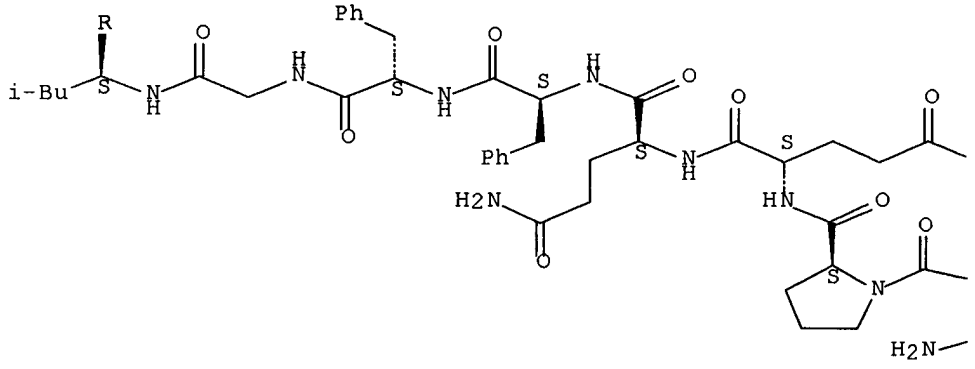

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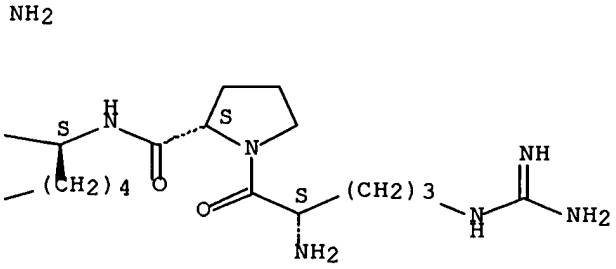

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